IEU (Epi)Genetics Journal Club

*“Only 30 minutes and you don't have to have read the paper, so please try to make it along!”*

We meet every Tuesday at 10:30am for 30 minutes in Barley House room BG7. Each week a volunteer presents a recently published epigenetics paper of their choice. For more information or to volunteer to present, send a note to one of the organizers:

Gemma Sharp ([gemma.sharp@bristol.ac.uk](mailto:gemma.sharp@bristol.ac.uk))

Matthew Suderman ([matthew.suderman@bristol.ac.uk](mailto:matthew.suderman@bristol.ac.uk))

Rota:

<https://docs.google.com/a/bristol.ac.uk/spreadsheets/d/14KhHDgbFl8uGqqoRqaAwf6eHvvYliKQsQB_y54vI48k/edit?usp=sharing>

March 26, 2019

**Presenter:** Matthew Suderman and Nancy McBride

Tomorrow morning (BG7, 10:30am), we visit the salad bar again (see previous announcement below). As you can readily verify, [Nancy](https://research-information.bristol.ac.uk/en/persons/nancy-mcbride(23d4b226-7ea1-4f77-9077-dcdab3f83443).html) and I have sourced only the freshest ingredients from the most reliable suppliers.

**Longitudinal analyses**

* Longitudinal DNAm changes and associations with treatment in [Parkinsons disease](https://www.ncbi.nlm.nih.gov/pubmed/30871403)
* [Chemotherapy](https://www.ncbi.nlm.nih.gov/pubmed/30867049) changes DNAm in blood.

**EWAS**

* [Fetal alcohol syndrome](https://www.ncbi.nlm.nih.gov/pubmed/30873861) associated with DNAm of blood collected in childhood (after age 5)
* [Opiod dependence](https://www.ncbi.nlm.nih.gov/pubmed/30874594) associated with DNAm in blood.
* [Allergic sensitisation](https://www.ncbi.nlm.nih.gov/pubmed/30876376) associated with DNAm in blood in childhood.
* [Shift work](https://www.ncbi.nlm.nih.gov/pubmed/30879037) associated with DNAm and epigenetic age in blood.
* [Maternal age](https://www.ncbi.nlm.nih.gov/pubmed/30879397) with DNAm in blood collected in adulthood.
* [Orofacial cleft](https://www.ncbi.nlm.nih.gov/pubmed/30870065) associated with DNAm from blood spots collected at birth (includes VTRNA2-1 gene)
* [Kidney function in HIV](https://www.ncbi.nlm.nih.gov/pubmed/30893429) associated with DNAm in blood.

**EWAS comparisons**

* Prenatal and own smoking DNAm associations in blood enriched in [lung tumour](https://www.ncbi.nlm.nih.gov/pubmed/30872662) DNAm differences.
* Associations of [colorectal cancer and of obesity](https://www.nature.com/articles/s41598-019-41616-0) similar in the DNAm of blood.

**Epigenetic age**

* An even larger [GWAS of epigenetic age acceleration](https://www.biorxiv.org/content/10.1101/585299v1) (n= 13,493) identifies a few novel genetic associations.

**Epigenetic variation**

* 'Epivariations' in blood DNAm linked to [autism and schizophrenia](https://www.ncbi.nlm.nih.gov/pubmed/30900359) (these are like rare variants)

**Cross-tissue comparisons**

* CpG site correlations between [placenta and cord blood](https://www.ncbi.nlm.nih.gov/pubmed/30885044) DNAm.

**Mechanism**

* Fumaric acid esters are highly effective immunomodulators in patients with [multiple sclerosis](https://www.ncbi.nlm.nih.gov/pubmed/30698680). This effect appears to be due to DNA methylation changes in brain-homing CCR6+ CD4 and CD8 T cells.
* Vitamin intake and genetic variation within DNMT3L interact to influence [cognitive decline](https://www.ncbi.nlm.nih.gov/pubmed/30877840).
* Letter to the editor discusses [our study](https://www.ncbi.nlm.nih.gov/pubmed/29860346) of persistence of prenatal smoking DNAm effects in connection with a link between [DRD1 and lung cancer](https://www.ncbi.nlm.nih.gov/pubmed/30879057) .

**Methods**

* [Bigmelon](https://www.ncbi.nlm.nih.gov/pubmed/30875430) is a tool for normalizing and analysing large DNAm datasets

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March 19, 2019

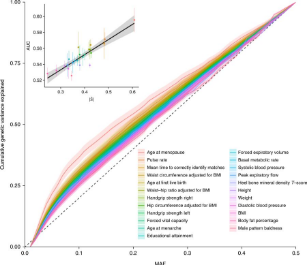
**Presenter:** Charlie Hatcher

This week at (epi)genetics journal club, Charlie Hatcher will be discussing the recent outputs of the #Visscher group

# **Signatures of negative selection in the genetic architecture of human complex traits**

<https://www.nature.com/articles/s41588-018-0101-4>

They introduce BayesS, a method to infer the action of natural selection on the genetic variants underlying a complex trait. Join us in **BG7 at 10:30 tomorrow** where we will be continuing our in-depth and Vissch-ous discussion about whether the plot below is a GREAT or TERRIBLE example of *#datavis*.



We will be having one vote on this, apart from Tom and I, who will get 3 #PeoplesVote.

March 12, 2019

**Presenter:** Matthew Suderman

Tomorrow morning (10:30am, BG7) is all about variety. We will depart from our normal procedure of discussing a recent publication and instead discuss a number of recent findings reported in the epigenetics literature. Delectable specifics are still being determined based on the following list, [sometimes so much choice is agonising](https://en.wikipedia.org/wiki/Overchoice) …

**Methods**

* Recommendations for handling cellular heterogeneity in [buccal DNAm](https://www.ncbi.nlm.nih.gov/pubmed/30821575).
* How to use public resources for [causal inference](https://www.ncbi.nlm.nih.gov/pubmed/30832291) in Epigenetic Epidemiology of Neurodevelopment and Mental Health (by Esther, Caroline and Doretta).
* [Long-read nanopore sequencing](https://www.ncbi.nlm.nih.gov/pubmed/30793194) identifies new imprinted regions in mouse.

**Candidate gene studies**

* [BDNF](https://www.ncbi.nlm.nih.gov/pubmed/30831210) associated with combat and exercise in veterans.

**EWAS**

* [Air pollution](https://www.ncbi.nlm.nih.gov/pubmed/30826615) in cord and placenta.
* [Air pollution](https://www.ncbi.nlm.nih.gov/pubmed/30819252) in adult peripheral blood.
* [Alcohol use disorder](https://www.ncbi.nlm.nih.gov/pubmed/30830696) associated with CpG sites associated with brain insular surface area.
* [Orofacial clefts](https://www.ncbi.nlm.nih.gov/pubmed/30832715) and newborn blood.   
  Fail to replicate findings based on [ALSPAC](https://doi.org/10.2217/epi-2018-0091) and the [Cleft Collective](https://www.ncbi.nlm.nih.gov/pubmed/28603561).
* [Preterm birth](https://www.ncbi.nlm.nih.gov/pubmed/30833390) and maternal blood.   
  Includes whole genome sequencing and RNA-seq.
* [Periodontitis](https://www.ncbi.nlm.nih.gov/pubmed/30760334) in blood, buccal and adipose tissue (Twins UK).
* [Childhood lung function and risks of asthma and COPD](https://www.ncbi.nlm.nih.gov/pubmed/30765504) in cord blood (meta-analysis of 5 cohorts).   
  The approach used is prone to false positives.
* [BMI and adolescent](https://www.ncbi.nlm.nih.gov/pubmed/30765773) peripheral blood leukocytes.   
  No tests survive adjustment for multiple tests, but functions of top genes 'make sense'.
* [Socio-economic position](https://www.ncbi.nlm.nih.gov/pubmed/30771258) in young adult blood.  
  2546 associations! Study performed in a non-affluent Philippine population.
* [Paternal pre-pregnancy obesity](https://www.ncbi.nlm.nih.gov/pubmed/30773972) and offspring cord blood.  
  Observed sex-specific associations. However, strongest association TAPBP was not replicated.
* [Insulin resistance](https://www.ncbi.nlm.nih.gov/pubmed/30792424) and peripheral blood.  
  798 CpG site associations observed!
* [Hepatic fat](https://www.ncbi.nlm.nih.gov/pubmed/30796027) and peripheral blood.  
  Observe 22 CpG site associations in 3,400 European, 401 Hispanic and 724 African ancestry participants.
* [Folic acid supplementation](https://www.ncbi.nlm.nih.gov/pubmed/30777123) during pregnancy (RCT) linked to differentially methylated regulator of ZPF57 in cord blood.

**DNAm scores**

* [BMI score](https://www.ncbi.nlm.nih.gov/pubmed/30842548) associated with health and disease in [LBC](https://www.lothianbirthcohort.ed.ac.uk/).

**DNAm age**

* [Developmental stage at least partially independent](https://www.ncbi.nlm.nih.gov/pubmed/30842553) of DNAm age in mammalian neural retina.
* Y-chromosome derived DNAm age is different from autosomally-derived DNAm age.  
  DNAm levels tend to increase with age, accelerate in the oldest individuals and associate negatively with mortality.

**Longitudinal DNAm**

* [Generalized estimating equestion (GEE) models](https://www.ncbi.nlm.nih.gov/pubmed/30764717) used to investigate smoking and DNAm at two time points.  
  Smokers tended to have greater DNAm change which was almost always linked to reduced DNAm levels.

March 5, 2019

**Presenter:** Matthew Suderman

With genetic testing of "healthy" individuals becoming a potential new tool for clinicians and direct-to-consumer genetic testing already readily available, the interpretation of the effects of all genetic variants is becoming extremely important. Rare disease studies often suffer from the fact they ascertain "unhealthy" individuals, which may bias results away from the null, whereas population cohorts often suffer from the opposite effects. There has generally been a disconnect between genetics studies within each domain, but as population cohort sample sizes with genetic data continue to rise, this may begin to rapidly change... Tomorrow we'll be discussing a paper that re-assessed rare variants discovered in a clinical/rare disease study setting within UK biobank. Join us tomorrow in BG7 at 10:30.

Paper:

[Wright et al. Assessing the Pathogenicity, Penetrance, and Expressivity of Putative Disease-Causing Variants in a Population Setting. February 2019](https://www.sciencedirect.com/science/article/pii/S0002929718304683?via%3Dihub#bib54)

February 27, 2019

**Presenter:** Sarah Watkins

The skeletons you've been hiding in your closets are about to be revealed. Garg et al. (2018) have recently identified a set of correlated but highly variably methylated regions spread throughout the genome. The variation appears to be environmentally induced with little influence from genotype. By experiment the authors uncovered many naughty secrets about the environments frequented by a group of genetically similar fibroblasts. Join us tomorrow when Sarah Watkins will reveal further salacious details (10:30am in BG7):

Garg, P., Joshi, R. S., Watson, C., & Sharp, A. J. (2018). A survey of inter-individual variation in DNA methylation identifies environmentally responsive co-regulated networks of epigenetic variation in the human genome. PLoS genetics, 14(10), e1007707.

February 19, 2019

**Presenter:**  Ashley Budu-Aggrey

PheWAS give the opportunity for researchers to assess the association between genetic variants and a large number of phenotypes. Combining this with polygenic risk scores could provide a powerful method to evaluate how the genetic basis of a disease relates to other traits. Tomorrow, Ashley will lead the discussion on an application of this in a cancer setting and the implications of the findings. Join us in BG7 at 10:30.

Paper:

[Lars G. Fritsche et al. Association of Polygenic Risk Scores for Multiple Cancers in a Phenome-wide Study: Results from The Michigan Genomics Initiative. June 2018](https://www.sciencedirect.com/science/article/pii/S0002929718301332?via%3Dihub)

February 12, 2019

**Presenter:** Matthew Suderman

Tomorrow morning (10:30am, BG7) we'll compare dying vs ageing.

To get us into the mood, we'll do a little test aimed at differentiating between normal ageing and dementia (adapted from [here](https://www.alztennessee.org/help/caregiver-support/caregiver-resource-library/dementia-vs-normal-aging)):

1. **Memory**: Do you temporarily forget names or do you forget familiar names?
2. **Orientation**: Do you forget why you entered a room or do you forget how to get home?
3. **Mental tasks**: Do you make mistakes following a recipe or are you unable to follow a recipe?
4. **Daily tasks**: Do you sometimes need help with the TV remote or are you unable to use the remote?
5. **Speaking**: Do you sometimes struggle to find the right word or do you have trouble forming logical sentences?
6. **Judgement**: Do you sometimes make questionable purchases or do you often give money away excessively?
7. **Mood**: Are you irritable when routines are changed or are you becoming increasingly withdrawn and suspicious?

I don't know about you, but I can often answer yes to both cases for all 7 questions! ... well except the checkbook. If you still use one of those *and* you balance it, then you're probably mentally sharper than those half your age who don't.

Tomorrow we'll see what DNA methylation has to say about the differences between ageing and mortality:

Lund JB, Li S, Baumbach J, Svane AM, Hjelmborg J, Christiansen L, Christensen K, Redmond P, Marioni RE, Deary IJ, Tan Q. [DNA methylome profiling of all-cause mortality in comparison with age-associated methylation patterns](https://www.ncbi.nlm.nih.gov/pubmed/30736859). Clin Epigenetics. 2019 Feb 8;11(1):23.

There's been a lot of epigenetics work published in the last few weeks:

* DNA methylation age
  + A new DNA methylation clock, [GrimAge](https://www.ncbi.nlm.nih.gov/pubmed/30669119), improves prediction of lifespan and 'healthspan'.
  + A longitudinal study in twins suggests that DNA methylation age may be influenced by [environment in old age](https://www.ncbi.nlm.nih.gov/pubmed/30704927).
* Assisted reproductive technologies
  + Imprinting disorders linked to [assisted reproductive technologies](https://www.ncbi.nlm.nih.gov/pubmed/30732658) likely take place just after fertilization.
* Pregnancy
  + [Maternal obesity in pregnancy](https://www.ncbi.nlm.nih.gov/pubmed/30732639) is linked to gene expression and DNA methylation changes in the adiponectin and leptin systems of the human placenta.
* Circadian rhythm
  + A fairly comprehensive review of [circadian rhythms and gene regulation](https://www.ncbi.nlm.nih.gov/pubmed/30721705).
  + DNA methylation is associated with [insufficient sleep](https://www.ncbi.nlm.nih.gov/pubmed/30718923).
* Fundamentals of DNA methylation
  + [Hypomagnetic fields](https://www.ncbi.nlm.nih.gov/pubmed/30718529) reduce the ability of cells to differentiate and disregulate DNMT3b reducing DNA methylation levels.
  + [Increased promoter CpG density](https://www.ncbi.nlm.nih.gov/pubmed/30709850) enhances gene activity *independently of DNA methylation*.
  + Specific CpG sites ('traffic lights') are better [predictors of gene activity](https://www.ncbi.nlm.nih.gov/pubmed/30709331) than overall promoter methylation.
  + The [best peripheral surrogate for brain](https://www.ncbi.nlm.nih.gov/pubmed/30705257) (saliva, buccal or blood) really depends on the genomic region of interest.
* Prediction
  + [Bladder cancer can be predicted](https://www.ncbi.nlm.nih.gov/pubmed/30706728) by measuring the DNA methylation of two genes in urine.

Feb 5, 2019

**Presenter**: Matt Lee

Of course we all know the plethora of harmful phenotypes obesity is linked to, but a growing body of research suggests there are groups of people with a higher adiposity, that don't have increased risks of certain diseases or the metabolic profile many other obese individuals do. This is termed "favourable adiposity". There have now been alleles found to associate with a higher adiposity, but lower risk of type 2 diabetes! How can this be so?? - Matt Lee will be explaining this and much more to us tomorrow at 10:30 in BG7. Hope to see you there!

Paper:

[Yingjie Ji et al. Genome-Wide and Abdominal MRI Data Provide Evidence That a Genetically Determined Favorable Adiposity Phenotype Is Characterized by Lower Ectopic Liver Fat and Lower Risk of Type 2 Diabetes, Heart Disease, and Hypertension. Diabetes 2019](http://diabetes.diabetesjournals.org/content/68/1/207.long)

Jan 29, 2019

**Presenter**: Matthew Suderman

If you love oranges, then you gotta love DNA methylation--without it, oranges don't [ripen](https://www.ncbi.nlm.nih.gov/pubmed/30635417).



But that's not what we'll be talking about tomorrow at 10:30am in BG7. Instead, we'll instead discuss a recently published argument that oranges, oops I mean SOCS3, is a possible drug target for oranges, sorry again I meant obesity (I'm going to go eat an orange):

Guo Q, Zheng R, Huang J, He M, Wang Y, Guo Z, Sun L, Chen P. [Using Integrative Analysis of DNA Methylation and Gene Expression Data in Multiple Tissue Types to Prioritize Candidate Genes for Drug Development in Obesity.](https://www.ncbi.nlm.nih.gov/pubmed/30619480) Front Genet. 2018 Dec 19;9:663.

... as well as other recent news in epigenetics:

* [Guide Positioning Sequencing](https://www.ncbi.nlm.nih.gov/pubmed/30670627) is better than Whole Genome Bisulfite Sequencing.
* [Education attainment](https://www.ncbi.nlm.nih.gov/pubmed/30631468) is associated with DNA methylation at 11 CpG sites independently of smoking status.
* [Oxytocin receptor methylation](https://www.ncbi.nlm.nih.gov/pubmed/30624029) appears to modulate oxytocin effects on human brain activity during social interaction.
* [Horvath's](https://www.ncbi.nlm.nih.gov/pubmed/30587240) [PhenoAge](https://www.ncbi.nlm.nih.gov/pubmed/29676998) does not capture the [effects of substance use on mortality](https://www.ncbi.nlm.nih.gov/pubmed/30650672).
* Brain-region specific DNA methylation and chromatin accessibility are enriched with loci associated with [neuropsychiatric traits](https://www.ncbi.nlm.nih.gov/pubmed/30643296) (analysis based on WGBS, RNA-seq and ATAC-seq profiles from 12 individuals).
* [Myocardial infarction](https://www.ncbi.nlm.nih.gov/pubmed/30587240) appears to induce DNA methylation changes at 9 CpG sites in blood.

Jan 22, 2019

**Presenter:** Simon Haworth

At ASHG 2018 one of the main focuses was on diversifying the populations we use in genetics studies. There are many benefits to this, but some analytical hurdles must be overcome. In the journal clubtomorrow, Simon Haworth will describe a new method that looks to estimate heritability in admixed populations by adapting LD score regression.

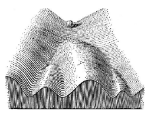
Paper:

[Lou et al. Estimating heritability of complex traits in admixed populations with summary statistics bioRxiv. 2018](https://www.biorxiv.org/content/biorxiv/early/2018/12/22/503144.full.pdf)

Jan 15, 2019

**Presenter:** Matthew Suderman

What am I? Am I at any moment simply a point in [Waddington's epigenetic landscape](https://books.google.co.uk/books/about/The_Strategy_of_the_Genes.html?id=odl1AwAAQBAJ&printsec=frontcover&source=kp_read_button&redir_esc=y#v=onepage&q&f=false) differentiating downhill toward the drop-off?



And if I somehow manage to fight the slope and move back uphill to a previous location, have I achieved anything of merit or am I exactly as I was at the earlier time?

And if I manage to reach a location previously occupied by someone else, do I take their identity? This is the question of [The Epigenetic Cloning Agency led by Jonathon Keats](https://www.livescience.com/37037-epigenetic-cloning-conceptual-art-keats.html). Keats proposes environmental exposures in the form of carefully designed tinctures for reaching locations on Waddington's landscape occupied by famous people. His Jesus Christ tincture, for example, includes omega-3 fatty acids ("he likely at a lot of fish"), iron ("nails were involved") and a generous dose of placebo ("the amount of faith ... was vast").

Tomorrow morning (BG7, 10:30am), Nancy McBride will help us consider this further, at the level of single cells. She will review what we are learning about how cells travel on the epigenetic landscape via the many "epilayers" of gene regulation. She will describe divergence between epigenetic and transcriptomic cell states, temporal trajectories of regulation, and regulatory diversity. By the time she is done, you may even begin to question the meaning of 'cell type'.

Shema E, Bernstein BE, Buenrostro JD.  [Single-cell and single-molecule epigenomics to uncover genome regulation at unprecedented resolution](https://www.ncbi.nlm.nih.gov/pubmed/30559489). Nat Genet. 2019 Jan;51(1):19-25.

Jan 8, 2019

**Presenter:** Laura Corbin

Very happy new year! For the first (epi)genetics journal club of 2019 Laura Corbin will be walking us through what may be wrong with using the model implemented in GCTA to estimate SNP heritability and provide us with another method.

Paper:

[Speed et al. Reevaluation of SNP heritability in complex human traits. Nat Gen 2017](https://www.nature.com/articles/ng.3865#f3)

See you there at the normal time of 10:30 in BG7.

For those interested:

The debate of the correct method to estimate SNP heritability has been going on for a few years now, see: [Improved heritability estimation from genome-wide SNPs](https://www.ncbi.nlm.nih.gov/pubmed/23217325) and the responses to it. They also debate the best method to estimate it from summary statistics: [SumHer better estimates the SNP heritability of complex traits from summary statistics](https://www.nature.com/articles/s41588-018-0279-5).

([slides](https://drive.google.com/open?id=1CxLGY9I2OutH4-CcQsbl655OezDF6PUi))

Dec 18, 2018

**Presenter**: Sam Neaves

Tomorrow morning (BG7, 10:30am) Sam Neaves will tell us about his PhD work on subgroup discovery in biological data using ... [Prolog](https://en.wikipedia.org/wiki/Prolog)! Prolog is a declarative computer language which means that a Prolog script is simply a set of facts and rules. This is different from language like R where the script explicitly tells the computer exactly how to complete a task.

... One of the most satisfying moments of my time in Computer Science was creating my own logic programming language similar to Prolog and using it to solve logic puzzles ... sigh ... oops, sorry, got a bit distracted there!

Sam will discuss how to use this approach to perform enrichment analyses and bumphunting in DNA methylation data and to finding subgroups of microbes in a microbiome dataset.

A [copy of his thesis chapter](https://drive.google.com/open?id=1opMvk5cevh4qw5scQsR2Dvxch22ODLvM) is available in case you'd like to take a peak.

Dec 11, 2018

**Presenter**: Ruth Mitchell

Tis the season to be jolly and tis the season of common cold and flu infections! To help deal with this at (epi)genetics journal club this week we're going to be learning a lot more about our defence mechanisms against infection. Ruth Mitchell will be explaining how variation amongst innate and adaptive immune cell parameters may be brought about by environmental and genetic factors.

Paper:

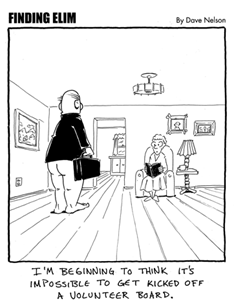
[Etienne Patin et al. Natural variation in the parameters of innate immune cells is preferentially driven by genetic factors. Nature Immunology 2018](https://www.nature.com/articles/s41590-018-0049-7#Sec1)

Dec 4, 2018

Unfortunately we'll need to cancel the journal club meeting tomorrow. We will resume next week Tuesday.

In the meantime, we're looking for volunteers to present in the new year. It's very easy to volunteer, just add your name next to a date in the spreadsheet below (which also contains a tab listing recommended papers, however you are certainly welcome to select something else):

<https://docs.google.com/spreadsheets/d/14KhHDgbFl8uGqqoRqaAwf6eHvvYliKQsQB_y54vI48k/edit?usp=sharing>



Nov 27, 2018

**Presenter:** Riccardo Marioni

Tomorrow morning (10:30am in BG7), Riccardo Marioni will be presenting a couple of his excellent recent papers. See below. Minutes ago he stated in front of 60 witnesses that "all I can think of is death and sex, can anyone think of anything else?". Clearly his presentation is sure to be exciting.

(disclaimer: I provide no context for his statement so cannot be accused of taking his words out of context)

Olova N, Simpson DJ, Marioni RE, Chandra T.  [Partial reprogramming induces a steady decline in epigenetic age before loss of somatic identity](https://www.ncbi.nlm.nih.gov/pubmed/30450724). Aging Cell. 2018 Nov 18:e12877.

Daniel Trejo Banos, Daniel L McCartney, Tom Battram, Gibran Hemani, Rosie M Walker, Stewart W Morris, Qian Zhang, David J Porteous, Allan F. McRae, Naomi R Wray, Peter M Visscher, Chris S Haley, Kathryn L Evans, Ian J Deary, Andrew M McIntosh, Riccardo E Marioni, Matthew R Robinson. [Bayesian reassessment of the epigenetic architecture of complex traits](https://www.biorxiv.org/content/early/2018/11/14/450288)

bioRxiv 450288; doi: https://doi.org/10.1101/450288

Nov 20, 2018

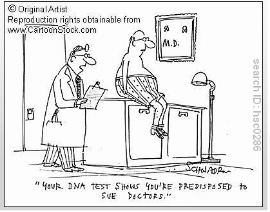
**Presenter:** Matthew Suderman

We finally have it, genome-wide DNA methylation profiles of a single individual over several months. Personalized medicine, here we come!

Tomorrow morning (10:30am in BG7), I will present the analysis of 28 whole-genome DNA methylation and 57 gene expression profiles from blood collected from the same person across 36 months:

Chen R, Xia L, Tu K, Duan M, Kukurba K, Li-Pook-Than J, Xie D, Snyder M. [Longitudinal personal DNA methylome dynamics in a human with a chronic condition](https://www.ncbi.nlm.nih.gov/pubmed/30397358). Nat Med. 2018 Nov 5.

To get you in the mood, below are some thoughts about the great hopes we have for technology and omics integration into medicine:





Incidentally, graphics on the [Institute for Systems Biology](https://systemsbiology.org/research/p4-medicine/) website suggests they may be mining the minds of infants for the secrets of personalised medicine:



And, finally, in other actual epigenetics news:

* A systematic mouse study suggests that [non-genetic inheritance linked to the Avy allele in Agouti mice is likely an exception than a general mechanism for non-genetic inheritance](https://www.sciencedirect.com/science/article/pii/S0092867418312558).
* [DNA methylation biomarkers of lung cancer in blood](https://www.ncbi.nlm.nih.gov/pubmed/30425263) have been discovered in the Norwegian Women and Cancer cohort study.
* [Single-cell chromatin profiling](https://www.ncbi.nlm.nih.gov/pubmed/29706550) shows increased variation with age, both between individuals as well as between cells within the same individual.
* [Nearly all disease-associated DNA repeats co-localise with chromatin domain boundaries](https://www.ncbi.nlm.nih.gov/pubmed/30173918) (Fragile X is a disease example).
* There is [a new epigenetic clock for mice](https://www.ncbi.nlm.nih.gov/pubmed/30427307) that better estimates age across the entire mouse lifespan.
* [DNA methylation at ANK1 is associated with Alzheimer's, Huntington's and Parkinson's disease](https://www.ncbi.nlm.nih.gov/pubmed/30439595) in the brain but in a region- and disease-specific manner.

([slides](https://drive.google.com/open?id=1nytpLLyW8GkR_VGLhIDcZfErWT4S5GzYb1rsUZYXxcQ))

Nov 13, 2018

**Presenter**: James Staley

This week at (epi)genetics journal club James Staley will be presenting the paper below that uses a new framework to identify interactions using UK biobank as well as introducing a new exciting plot - the "Manhattan Sunset"!

Paper:

[Young et al. Identifying loci affecting trait variability and detecting interactions in genome-wide association studies](https://www.nature.com/articles/s41588-018-0225-6#Sec12)

Nov 6, 2018

**Presenter**: Lea Perret

Tomorrow morning (BG7, 10:30am), Lea Perret will give us a tour through 3 publications on peer victimization:

1. Geoffroy, M. C., Boivin, M., Arseneault, L., Turecki, G., Vitaro, F., Brendgen, M., ... & Côté, S. M. (2016). Associations between peer victimization and suicidal ideation and suicide attempt during adolescence: results from a prospective population-based birth cohort. *Journal of the American Academy of Child & Adolescent Psychiatry*, *55*(2), 99-105.
2. Geoffroy, M. C., Boivin, M., Arseneault, L., Renaud, J., Perret, L. C., Turecki, G., ... & Tremblay, R. E. (2018). Childhood trajectories of peer victimization and prediction of mental health outcomes in midadolescence: a longitudinal population-based study. *Canadian Medical Association Journal*, *190*(2), E37-E43.
3. Perret, LC, Orri, M, Boivin, M, Ouellet-Morin, I, Côté, SM, Tremblay, R, Renaud, J, Turecki, G, Geoffroy, MC. Concurrent and longitudinal associations of cyber versus face-to-face victimization to suicidal ideation and attempt during adolescence. Submitted to *Lancet Psychiatry*.

Lea Perret is a PhD student in Mental Health Research at the [Department of Psychiatry at McGill University](https://www.mcgill.ca/psychiatry/) in Montreal QC where she is being supervised by [Dr Geoffroy](https://douglas.research.mcgill.ca/marie-claude-geoffroy) and [Dr Turecki](https://douglas.research.mcgill.ca/gustavo-turecki). She completed a masters in neuroscience on animal models of depression in early-life and is now studying the effects of peer victimization in childhood and adolescence on suicidality and depression. While in Bristol, she will be investigating associations of bullying, suicidal ideation and depressive ideas in DNA methylation in the 1958 British Birth Cohort.

Lea will be visiting the IEU until Nov 16 and making the BS10 office even more fabulous.

Oct 30, 2018

**Presenter:** Chris Zheng

This weeks (epi)genetic journal club **will be at the slightly later time of 2pm**, to accommodate the jet lag of our ASHG gang!\*

Chris Zheng will be presenting [Emilsson V et al. Co-regulatory networks of human serum proteins link genetics to disease](https://www.ncbi.nlm.nih.gov/pubmed/30072576)

Please join us in **BG7** to pile through Tom Battram's stash of peanut butter M&Ms and other delectable American snacks\*\*

Oct 23, 2018

**Presenter:** Matthew Suderman

Is consortia work getting you down? Does the word 'consortium' bring to mind passive-aggressive email exchanges, scripts that worked fine until someone else used them, watered-down manuscripts that even you wouldn't read, international summits to negotiate authorship, or fantasies about swapping co-authors for reviewer number 3? Well Mario Bauer has your back. In a recent review, he suggests leaving consortia work to our more diplomatic genetics colleagues and doing something quite different in epigenetics. Join us tomorrow (10:30am, BG7) to discuss his proposal:

Bauer M. [Cell-type-specific disturbance of DNA methylation pattern: a chance to get more benefit from and to minimize cohorts for epigenome-wide association studies.](https://www.ncbi.nlm.nih.gov/pubmed/29506027) Int J Epidemiol. 2018 Mar 1.

In other epigenetics news:

* Childhood abuse is associated with [human sperm DNA methylation](https://www.ncbi.nlm.nih.gov/pubmed/30279435).
* [Caenorhabditis elegans sperm carry epigenetic memory](https://www.ncbi.nlm.nih.gov/pubmed/30333496) of both spermatogenesis and oogenesis.
* DNA sequence appears to determine whether a DNA molecule prefers to [loop or condense](https://www.ncbi.nlm.nih.gov/pubmed/30032232), but this can be modified by the addition of DNA methylation.

([slides](https://docs.google.com/presentation/d/1sAkAJohUFlK93xCg96O5fW5t9qZbKPeBFDNfXvlMCoI/edit?usp=sharing))

Oct 16, 2018

**Cancelled because of ASHG.**

Oct 9, 2018

**Presenter:** Doretta Caramaschi

If you passed by BG7 a couple of weeks ago, you may have heard some potentially disturbing [maniacal laughter](https://www.youtube.com/watch?v=WaIJKM0sjdo). It's what researchers tend to do when they ponder the [possibilities of CRISPR](https://doi.org/10.1016/S0140-6736(18)31653-2). Doretta's presentation about how it was used to edit DNA methylation to reverse [Fragile X Syndrome](https://en.wikipedia.org/wiki/Fragile_X_syndrome) generated so much discussion that we decided to continue this week (tomorrow, 10:30am in BG7).

Liu et al. [Rescue of Fragile X Syndrome Neurons by DNA Methylation Editing of the FMR1 Gene](https://www.ncbi.nlm.nih.gov/pubmed/29456084). Cell. 2018 Feb 22;172(5):979-992.e6.

Recent news in epigentics:

* EWAS in tissues other than blood
  + Acute [sleep loss](https://www.ncbi.nlm.nih.gov/pubmed/30140739) results in tissue-specific changes in DNA methylation (adipose and skeletal muscle).
  + Childhood abuse is associated with DNA methylation changes in [sperm](https://www.ncbi.nlm.nih.gov/pubmed/30279435).
  + [ELOVL5](https://www.ncbi.nlm.nih.gov/pubmed/30291282) investigated as an 'epigenetic' biomarker of [type 2 diabetes](https://www.ncbi.nlm.nih.gov/pubmed/30291282) in MZ twin blood and other tissues as well as in mice.
* EWAS of environmental exposure
  + [Air pollution in 4 European countries](https://www.ncbi.nlm.nih.gov/pubmed/30055357) is associated with DNA methylation.
  + [Pesticide exposure](https://www.ncbi.nlm.nih.gov/pubmed/30248838) in an agriculturally intense region in California is associated with DNA methylation.
* Investigating DNA methylation
  + A [genome-wide survey of DNA methylation inter-individual variation](https://www.ncbi.nlm.nih.gov/pubmed/30273333) has been published.
  + [Reanalysis](https://www.biorxiv.org/content/biorxiv/early/2018/08/01/381145.full.pdf) of a dataset finds that promoter DNA methylation usually represses gene expression, contradicting previous [findings](https://www.biorxiv.org/content/early/2018/08/01/381145).
* Epigenetic clocks
  + Epigenetic clocks have not worked well in [skin until](https://www.ncbi.nlm.nih.gov/pubmed/30048243) [now](https://www.ncbi.nlm.nih.gov/pubmed/30048243).
* Reviews
  + A review discusses the hypotheses smuggled into ['hypothesis-free' EWAS](https://www.ncbi.nlm.nih.gov/pubmed/30077874).
  + A [literature review](https://www.ncbi.nlm.nih.gov/pubmed/29506027) suggests that we should focus on studying the right cell type rather than increasing sample size.

Oct 2, 2018  
**Presenter:** Alice Carter

Back to genetics this week and we have Alice Carter talking to us about using polygenic risk scores for prediction of five common diseases and the possible utility of polygenic scores for identifying those at high risk of common diseases in the clinic:

[Amit Khera et al. Genome-wide polygenic scores for common diseases identify individuals with risk equivalent to monogenic mutations](https://www.nature.com/articles/s41588-018-0183-z)

Please join us in BG7 at 10:30 tomorrow to find out more!

Sept 25, 2018

**Presenter:** Doretta Caramaschi

Imagine that you're supervising a PhD student, and they just don't see things your way. You've tried every reasonable solution, so you decide to try the spray your mate in epigenetics gave you after last week's faculty whinge. Next supervisory meeting, you spray a small amount on their keyboard when they're not looking and a few days later they're good as gold.



Sound too good to be true? Join us tomorrow (10:30am in BG7) to hear Doretta Caramaschi explain how to use DNA methylation editing tools to reverse [Fragile X Syndrome](https://en.wikipedia.org/wiki/Fragile_X_syndrome) in neurons. She might even be induced to disclose how we might deliver treatments like this by aerosol spray.

Liu et al. [Rescue of Fragile X Syndrome Neurons by DNA Methylation Editing of the FMR1 Gene](https://www.ncbi.nlm.nih.gov/pubmed/29456084). Cell. 2018 Feb 22;172(5):979-992.e6.

Recent news in epigentics:

* An EWAS of 1132 individuals of all [28 million CpG sites](https://www.ncbi.nlm.nih.gov/pubmed/30242228) uncovered associations with major depressive disorder!
* [Early life but not adult socio-economic position](https://www.ncbi.nlm.nih.gov/pubmed/30016711) is associated with epigenetic age.
* There is a histone methylation signature of inflammation in [Crohn's disease](https://www.ncbi.nlm.nih.gov/pubmed/30232290).

Sept 18, 2018

**Presenter:** Denis Baird

The suspense is over! Today, Denis Baird will be presenting:

"Integrative analysis of omics summary data reveals putative mechanisms underlying complex traits" from Yang Wu and colleagues (2018)

See you in BG7 at 10:30!

Sept 11, 2018

**Presenter:** Esther Walton

**Headline** A large meta-analysis of DNA methylation implicates axon guidance in depression

Hear Esther Walton tell all about it tomorrow at 10:30am in BG7:

Story Jovanova et al. [DNA Methylation Signatures of Depressive Symptoms in Middle-aged and Elderly Persons: Meta-analysis of Multiethnic Epigenome-wide Studies](https://www.ncbi.nlm.nih.gov/pubmed/29998287). JAMA Psychiatry. 2018 Sep 1;75(9):949-959.

[Axon guidance](https://en.wikipedia.org/wiki/Axon_guidance) is the mysterious process by which neurons grow axons to connect with other neurons. We know that the tip of the axon has a growth cone that "sniffs" around for molecular signals that either attract or repel. This much makes sense but we know little about why or how axon growth is so precise. You can actually watch it happen on [youtube](https://www.youtube.com/watch?v=F_NHOCx9AMs) (the comment section contains a cautionary tale about public engagement).

Other news in epigenetics:

* [Whole-genome bisulfite sequencing](https://www.ncbi.nlm.nih.gov/pubmed/30093547) is getting a lot cheaper.
* There is a need for more sensitive ways to [verify ages of refugees](https://www.nature.com/articles/d41586-018-06121-w).
* [Age associations](https://www.ncbi.nlm.nih.gov/pubmed/30079798) in DNA methylation and hydroxymethylation are largely distinct in mouse blood.
* [Cancer and aging](https://www.ncbi.nlm.nih.gov/pubmed/29893918) induce similar DNA methylation changes in multiple tissues.
* DNA methylation associated with [frailty index](https://www.ncbi.nlm.nih.gov/pubmed/30136078) in elderly twins.
* DNA methylation associations with [food allergy in CD4+T cells](https://www.ncbi.nlm.nih.gov/pubmed/30120223) possibly due to gene-environment interactions.
* There is greater DNA methylation variability in [rheumatoid arthritis](https://www.ncbi.nlm.nih.gov/pubmed/30176915#)-discordant MZ twins.
* [Gestational diabetes mellitus](https://www.ncbi.nlm.nih.gov/pubmed/30185669) is associated with DNA methylation in offspring during childhood (DNBC study).
* [Pollution](https://www.ncbi.nlm.nih.gov/pubmed/29935799) is associated with placental DNA methylation (EDEN study).
* [Cold exposure](https://www.ncbi.nlm.nih.gov/pubmed/29988127) induces changes in sperm DNA methylation and enhances capacity to form mature active brown adipocytes.
* A small study of 5-hydroxymethylation observes differences in brains of [autism spectrum disorder](https://www.ncbi.nlm.nih.gov/pubmed/29790956).
* EWAS of [IQ](https://www.ncbi.nlm.nih.gov/pubmed/30166545) identifies association linked to DRD2 (IMAGEN study).

August 7, 2018

**Presenter**: Kim Burrows

**SCENE**: *14:02 pm,* ***last Monday****, the 30th July 2018. Our leading man Paul Yousefi\* had started the week on a high, having read the brilliant* [*response*](https://medium.com/@darren_dahly/an-open-letter-to-dr-eva-orsmond-20f5d2420672) *from some of the IEU's own to a* [*clickbaiting disaster*](https://www.irishmirror.ie/news/irish-news/overweight-pregnant-health-eva-orsmond-12979580) *by Dr Eva Osmond. His mood quickly turns as he begins his daily scroll through Vogue online, finding himself incensed at the latest travesty in the market of* [*epigenetic*](https://www.vogue.com/article/epigenetics-research-dna-gene-expression-smart-skin-care)*s miracle cures. Face creams had never worked for him! His musings are interrupted by the dulcet tone of Outlook, signalling the arrival of a new email.*

PY: Ooooh, journal club! My favourite extra-curricular activity! I wonder what’s in store this week?

*His heart starts to sink as he reads the title of the proposed article: "*[*The Importance of DNA Methylation of Exons on Alternative Splicing*](http://rnajournal.cshlp.org/content/early/2018/07/12/rna.064865.117)*". Why can’t he understand what those words mean!? Imposter Syndrome can only explain so much.*

PY: EXONS?! ALTERNATIVE SPLICING?! This is worse than trying to make sense of one of Matthew Lee's emails!

*Matthew Suderman suddenly appears in a double helix-tornado of smoke. He looks longingly at Trump Towers (the weights machine in their office), before deciding it's not worth asking how much use it's seen in his absence. After all, fragile masculinity can only take up so much of everyone's day.*

MS: Do not worry Paul Yousefi. I have foreseen, from Naples, that due to technical issues journal club is going to be pushed back a week. **Kim Burrows** will in fact be explaining all on **Tuesday 7th August at 10:30am in BG7.** You know, Nancy's email was littered with questionable content. Frankly, I can't believe Tom B gave her this responsibility in the first place.

PY: Oh thank goodness! That extra week will give me plenty of time to read the paper before journal club so there really is no excuse to not turn up with insightful queries and/or comments. Exon out homey!

MS: Vitello solleva!

**\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\***\* *our hero and saviour, the guardian of* [*Musical Randomisation*](https://open.spotify.com/user/yousefi.paul/playlist/1FQUGd7fwfTAJxGcTvDv7e?si=Rn1jZd43RqqzujqxuJ3c_g)*, the IEU Spotify playlist (please join and contribute).*

*\*\*still not indicative of real events. Matthew Suderman has not commanded the ability to apparate, from Naples or anywhere else. Matthew Lee, your emails are a treat; capital letters* are *overrated. Paul Yousefi, forgive us.*

*\*\*\*keep looking out for our upcoming screenplay "Academi-Uh?!"© 2018 German & Saunders Inc.*

*\*\*\*\*George, please fund this.*

July 31, 2018

**SCENE:** *Post-heatwave Monday morning, everyone has the slightly fresher look of people who slept in actual duvets - not just the sheet. Our two protagonists are hatching a plan.*

Tom B: Nancy, will you write this weeks epi(genetic) journal club email?

Nancy: Of course, Tom! As a PGR, I will do anything I can to enhance my profile in the IEU!

Tom B: Thanks Nancy, you are a credit not only to yourself, but to your supervisors and society as a whole \**sends paper entitled* "[The Importance of DNA Methylation of Exons on Alternative Splicing](http://rnajournal.cshlp.org/content/early/2018/07/12/rna.064865.117)" *by Ronna Shayevitch, Dan Askayo, Ifat Keydar and Gil Ast*\*

Nancy: Oh man, I'm going to struggle to link this paper's topic to the witty repertoire I had planned - discussing the Mitchell-Escher twitter [debate](http://www.wiringthebrain.com/2018/07/calibrating-scientific-skepticism-wider.html) regarding transgenerational epigenetic changes! Or to my original take on the so-called dystopian nightmare that is the [23&Me/GSK](https://www.theatlantic.com/science/archive/2018/07/big-pharma-dna/566240/) collaboration! Also...what do those words mean?

Tom B: That's what everyone can find out tomorrow **@ 10:30 am in BG7**, when **Kimberley Burrows** will reveal all!

Nancy: But what about the devastating news we have to share, who will break it to everyone?!

Tom B: I thought this much was obvious.

Nancy: JOURNAL CLUB IS CANCELLED FOR THE MONTH OF AUGUST BECAUSE MATTHEW SUDERMAN HAS TAKEN HIS CALF RAISES TO NAPLES

**See you in September folks!**

#spliceosome

\*\*\*this is not an actual interaction and was curated purely for entertainment purposes. Tom, please don't sue me.

\*\*\*\*this paper is paywalled hence a handy .zip file is attached.

\*\*\*\*\*please keep a lookout for my upcoming screenplay, "Academi-Uh?!"© 2018

July 24, 2018

**Presenter:** Lavinia Paternoster

Our genes are complex and have a wide variety of functions. These functions have been attributed to everything from our eating habits toour [criminal activities](https://www.independent.co.uk/news/uk/do-your-genes-make-you-a-criminal-1572714.html). Although these claims may be (at least in part) justified, we must do more to uncover the genes truly driving the discrepancies in human behaviour and disease. This week Lavinia Paternoster will present a paper that integrates 3 methods to try and identifycausal genes related to chronic obstructive pulmonary disease (COPD). So join us tomorrow at 10:30 in BG7 to find out more:

Lamontagne M. et al. [Leveraging lung tissue transcriptome to uncover candidate causal genes in COPD genetic associations](https://www.ncbi.nlm.nih.gov/pubmed/29547942)

July 17, 2018

**Presenter:** Paul Yousefi

This week our topic is placental meteorology. Naturally our presenter will be Paul Yousefi, widely known to have survived several months attached to a placenta under a variety of meteorological conditions. Tomorrow morning (BG7, 10:30am), he will tell us all about this experience as well as what recent scientific discoveries suggest about the epigenetic state of his placenta after he was finished with it.

Abraham E, Rousseaux S, Agier L, Giorgis-Allemand L, Tost J, Galineau J, Hulin A, Siroux V, Vaiman D, Charles MA, Heude B, Forhan A, Schwartz J, Chuffart F, Bourova-Flin E, Khochbin S, Slama R, Lepeule J; EDEN mother-child cohort study group. [Pregnancy exposure to atmospheric pollution and meteorological conditions and placental DNA methylation.](https://www.ncbi.nlm.nih.gov/pubmed/29935799) Environ Int. 2018 Sep;118:334-347.

You may also be interested in:

* Epigenetic-based omnigenic model of psychiatric disorders [discussed](https://www.ncbi.nlm.nih.gov/pubmed/29775682).
* [Stool DNA methylation](https://www.ncbi.nlm.nih.gov/pubmed/29542109) harbors a biomarker of colorectal cancer.
* Sperm epigenome modified and obesity risk reduced following [paternal cold exposure](https://www.ncbi.nlm.nih.gov/pubmed/29988127). Go Canada!
* [Large EWAS of depressive symptoms](https://www.ncbi.nlm.nih.gov/pubmed/29998287) published by CHARGE.
* DNA methylation [regulates alternative splicing](https://www.ncbi.nlm.nih.gov/pubmed/30002084).
* [Substantial immune cell contamination](https://www.ncbi.nlm.nih.gov/pubmed/29693419) in saliva, buccal and cervix samples revealed by DNA methylation-based cell count estimates.
* [Prenatal phthalate exposure](https://www.ncbi.nlm.nih.gov/pubmed/29957030) induces DNA methylation changes in imprinted genes.
* [New imprinted genes discovered](https://www.ncbi.nlm.nih.gov/pubmed/29957030) using the Illumina Infinium MethylationEPIC BeadChip.

([slides](https://drive.google.com/open?id=1l6Tw7wJrnmOUVW69nQnGmS_0cLT-T7os))

# June 26 - July 10, 2018

No journal club.

# June 19, 2018

**Presenter**: Matthew Suderman

**Blood** is being vindicated. It's been called 'peripheral', 'off-target but convenient', 'what we have', 'disgusting', etc. However, it was recently shown that [during 3 million years of our evolution, blood flow rates to the brain increased 6-fold while brain size increased only 3.5 times](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5108958/). To which blood responded: "Take that brain, still think you're the shining pinnacle of human evolution? You'd be little more than an colourless vegetable without me."

And tomorrow morning it continues (10:30am, BG7). We'll discuss evidence that our large genomic datasets derived from blood tell us more about brains and traits than our much smaller genomic datasets derived from the brain itself.

Qi T, Wu Y, Zeng J, Zhang F, Xue A, Jiang L, Zhu Z, Kemper K, Yengo L, Zheng Z; eQTLGen Consortium, Marioni RE, Montgomery GW, Deary IJ, Wray NR, Visscher PM, McRae AF, Yang J. [Identifying gene targets for brain-related traits using transcriptomic and methylomic data from blood](https://www.ncbi.nlm.nih.gov/pubmed/29891976). Nat Commun. 2018 Jun 11;9(1):2282.

([slides](https://drive.google.com/open?id=1kLSj2GfFLXkGPuS4R9fPVWp6GlDhTwEmbhPRukfd0Rw))

# June 12, 2018

**Presenter**: Carolina Borges

According to one report global warming may lead to parts of Europe turning into [deserts](https://www.independent.co.uk/news/world/europe/global-warming-turning-europe-into-desert-2100-mediterranean-spain-portugal-italy-sicily-turkey-a7383931.html) very soon! To help prepare you for this change I thought I would share a few facts you might not know about our favourite desert crossing animals, camels:

* They can run up to 40mph (67kph)
* They are known for spitting on people when they feel threatened – this spit also contains some of the contents of their stomach
* A camel noise was used to help voice Chewbacca in Star Wars
* Their popularity within the genetics community has led to a new method being named after them (CaMMEL)

For more camel facts visit [here](https://www.livescience.com/27503-camels.html). For more information on how to identify genes that are mediating the effect of SNPs from GWAS summary statistics using CaMMEL then come to BG7 at 10:30 tomorrow where Carolina Borges will present:

Park et al. [A Bayesian approach to mediation analysis predicts 206 causal target genes in Alzheimer's disease](https://www.biorxiv.org/content/early/2017/12/01/219428). biorxiv

# June 5, 2018

**Presenter**: Tom Battram

Tomorrow's meeting is all about bodily fluids and DNA methylation. In most genomics publications, we're usually pretty happy with analysis of one fluid, but this time we have three: saliva, urine and plasma. If it sounds like the authors have found some generous donors, consider this:

* An average male body has 17 litres of water outside of cells and a female body 11.5 litres.
* The human body produces over [30 different fluids](https://en.wikipedia.org/wiki/Body_fluid), many of them easily collected (some with a mop and bucket!).

Clearly the use of bodily fluids in genomics , as in [art](https://en.wikipedia.org/wiki/Body_fluids_in_art), has only just begun. If you're short on cash, you could even [sell some of your own](http://www.ehow.co.uk/how-does_5045598_getting-paid-donating-body.html) (including [this](https://www.openbiome.org/stool-donation/)) but not on [eBay](http://www.slate.com/articles/life/explainer/2012/11/glenn_beck_s_obama_pee_pee_hoax_is_it_legal_to_sell_your_own_urine.html?via=gdpr-consent).

Tomorrow morning (10:30am in BG7), Tom Battram will present the following:

Zaghlool et al. [Deep molecular phenotypes link complex disorders and physiological insult to CpG methylation](https://www.ncbi.nlm.nih.gov/pubmed/29325019). Hum Mol Genet. 2018 Mar 15;27(6):1106-1121.

# May 29, 2018

**Presenter**: Tom Richardson

The heritability heavyweights have been throwing punches back and forth like Ali and Frazier, see <https://twitter.com/djbalding/status/975862076928241664>. But this has given the rest of us the tools to uncover the genetic architecture of many traits. Now heritability analyses may also be able to identify disease relevant tissues. Giving a knockout explanation of this new method will be Tom Richardson in the ring that is BG7, tomorrow at 10:30:

Finucane et al. [Heritability enrichment of specifically expressed genes identifies disease-relevant tissues and cell types.](https://www.ncbi.nlm.nih.gov/pubmed/29632380) Nat Genet. 2018 Apr;50(4):621-629.

([slides](https://drive.google.com/open?id=11IDQPvJWPOd3d7CpKOrylPa9VpH0Z2MX))

# May 22, 2018

**Presenter**: Ryan Arathimos

If you haven't yet been introduced, it is time you met [**Tumor Necrosis Factor α**](https://en.wikipedia.org/wiki/Tumor_necrosis_factor_alpha), known on the street as Alpha Gene Tumor Killer and affectionately as TNF-α to friends. Meet the ruler of the cellular world. It's job title Proinflammatory Cytokine represents only the tip of its generific iceberg. It's nucleotides are positively pleiotropic: pathogen defence, tissue repair, tissue regeneration, organ development, appetite regulation, and many more. It plays key roles in all sorts of diseases including atherosclerosis, type 2 diabetes, many cancers, multiple sclerosis, Alzheimer's disease, major depression, psoriasis, and inflammatory bowel disease.

Importantly, TNF-α has a **longer Wikipedia page** (nearly 30 characters) than over 97% of UoB Academics with this distinction (including two IEU leads). Only six have longer pages, the longest belonging to David Nutt. In the spirit of reproducible science, the R script for this ground-breaking analysis is reproduced below.

And finally, TNF-α has effects on DNA methylation that are relevant to Coronary Heart Disease. Ryan Arathimos will tell us more about this tomorrow morning (10:30am in BG7):

Aslibekyan et al. [Association of Methylation Signals With Incident Coronary Heart Disease in an Epigenome-Wide Assessment of Circulating Tumor Necrosis Factor α.](https://www.ncbi.nlm.nih.gov/pubmed/29617535) JAMA Cardiol. 2018 Apr 4.

# May 15, 2018

**Presenter**: Dan Lawson

Archaeologists believe that people have been eating popcorn for thousands of years, but there have been more uses for it than just food, for example [Christmas tree decorations](https://www.gourmetgiftbaskets.com/Blog/post/popcorn-christmas-garlands.aspx). Tomorrow in BG7 at 10:30 Daniel Lawson will present an entirely new way to use Popcorn (may or may not just be the name of a Python package) to estimate transethnic genetic-correlation:

Brown BC et al. [Transethnic Genetic-Correlation Estimates from Summary Statistics](https://www.ncbi.nlm.nih.gov/pubmed/27321947)

We're back with epigenetics next week with Ryan Arathimos presenting:

Aslibekyan S et al. [Association of Methylation Signals With Incident Coronary Heart Disease in an Epigenome-Wide Assessment of Circulating Tumor Necrosis Factor α](https://www.ncbi.nlm.nih.gov/pubmed/29617535)

# May 8, 2018

**Presenter**: Hannah Elliott

DNA methylation patterns are apparently a little like the laws of a country:

- Initially, they tend to be consistent with some fabulous ideology. (Twins are born with identical methylation patterns)

- They define different organisations and their cooperation toward achieving world domination. (Cell types and organs owe their existence in large part to DNA methylation)

- Over time, laws tend to become complex in response to practicalities like greed, ignorance and politics. (Methylation patterns of twins diverge over the lifecourse in part due to environmental exposures)

- Wealth can reduce the negative impact of laws that favour the 1% (Just as an addiction to carcinogens induces well-defined DNA methylation patterns but has reduced health risks in high socio-economic individuals)

Tomorrow morning (BG7, 10:30am), Hannah Elliott will discuss all this and more:

Forest M, O'Donnell KJ, Voisin G, Gaudreau H, MacIsaac JL, McEwen LM, Silveira PP, Steiner M, Kobor MS, Meaney MJ, Greenwood CMT. [Agreement in DNA methylation levels from the Illumina 450K array across batches, tissues, and time](https://www.ncbi.nlm.nih.gov/pubmed/29381404). Epigenetics. 2018;13(1):19-32.

# April 24, 2018

**Presenter**: Gemma Sharp

And now, the final episode of our hijacking [saga](https://docs.google.com/document/d/11kXUsNAar4i0oApAMfHZkilucTjR9OsjhAo8H6RaQgs/edit):

Many years passed and our scientists managed to avoid being killed by hijackers. They, like the rest of homo sapiens, however, did not avoid the inevitable. Both died of natural causes while pondering the secrets of the universe. Both donated their bodies to science, and, needless to say, both had epigenetic clock profiles constructed. The geneticist had advanced age according to the PhenoAge clock. This made some sense because she died from complications related to bone cancer. The epigeneticist's PhenoAge was just about right. His cause of death was unknown. He did however have advanced age according to the original Horvath clock, an observation befitting a life of stress. The Hannam clock however indicated the opposite, a younger epigenetic age. Alas, in death he literally embodied the frustrating relationship of every epigeneticist with the epigenome.

Tomorrow morning (BG7, 10:30am), Gemma Sharp will introduce Horvath's new PhenoAge clock and discuss its relationship to the other epigenetic clocks. Of course, it will all make perfect sense ...

Horvath S, Raj K. [DNA methylation-based biomarkers and the epigenetic clock theory of ageing](https://www.nature.com/articles/s41576-018-0004-3). Nat Rev Genet. 2018 Apr 11.

# April 17, 2018

**Presenter**: Teri-Louise North

Robins C et al. [Testing Two Evolutionary Theories of Human Aging with DNA Methylation Data](https://www.ncbi.nlm.nih.gov/pubmed/28855307)

The [saga](https://docs.google.com/document/d/11kXUsNAar4i0oApAMfHZkilucTjR9OsjhAo8H6RaQgs/edit) continues with part 11:

The hunt for the scientists had taken the hijackers through numerous genetic and epigenetic articles and even to a conference. Their growing infatuation with the fields was apparent from their new topics of conversation. When discussing the appearance of the scientists to help in their investigation, the hijackers noted how the geneticist must be younger. However, one hijacker said that the geneticist’s youthful appearance may not be entirely explained by her chronological age. They began to discuss influences of differential aging between individuals in great depth. In a situation similar to departments across the world, the hijackers split into two groups: those arguing the greater contribution of genetics and those arguing that epigenetics played a greater role. Once the heated debate died down, one individual then asked a question for which none of the hijackers had an answer: why do we age? Interestingly, the combination of genetic and DNA methylation analysis has been used to try and understand theories for this exact question – Teri will explain more tomorrow!

# April 10, 2018

**Presenter**: David Hughes

Stephane E Castel et al. [Modified penetrance of coding variants by cis-regulatory variation shapes human traits](https://www.biorxiv.org/content/early/2018/01/08/190397)

Note: The paper that was scheduled to be presented (email sent 2 weeks ago) has changed.

Next week Teri Louise-North will be presenting the following paper:

Robins C et al. [Testing Two Evolutionary Theories of Human Aging with DNA Methylation Data](https://www.ncbi.nlm.nih.gov/pubmed/28855307)

Many of the hijackers were parents and had booked time off for the Easter holidays. They therefore decided to put capturing the scientists on hold until they had fulfilled their family duties, but will resume their mission next week. Whilst they’re away feel free to reacquaint yourselves with the previous episodes of the [saga](https://docs.google.com/document/d/11kXUsNAar4i0oApAMfHZkilucTjR9OsjhAo8H6RaQgs/edit).

# March 27, 2018

**Presenter**: Lotte Houtepen

The [saga](https://drive.google.com/open?id=11kXUsNAar4i0oApAMfHZkilucTjR9OsjhAo8H6RaQgs) continues ... As time went on, the hijackers became more and more desperate to catch our epigeneticist: they distributed wanted posters, attached "lost epigeneticist" signs to telephone poles, passed photos around at epigenetics meetings, and tweeted threats. The other day our epigeneticist was wracking his brain for a solution when he spotted the recent Marzi et al. paper published in the American Journal of Psychiatry:  
  
Marzi, et al. [Analysis of DNA Methylation in Young People: Limited Evidence for an Association Between Victimization Stress and Epigenetic Variation in Blood](https://www.ncbi.nlm.nih.gov/pubmed/29325449). Am J Psychiatry. 2018 Jan 12:appiajp201717060693.  
  
[Incidentally Lotte Houtepen will present this paper tomorrow morning at 10:30am BG7.]  
  
The authors take the quite controversial stance that "epigenetic epidemiology is not yet well matched to experimental, nonhuman models in uncovering the biological embedding of stress". This gave our epigeneticist an idea. He called up one of his friends at MI5, told him the full story and together they hatched a plan. A week later, a letter to the editor appeared in the highly respected Annals of Epigenetics responding to the controversial claims of Marzi et al. The letter included a recent photo of the epigeneticist and contact details for certain countryside lodge in Glencoe.   
  
Next week Tuesday the university is closed so there will be no journal club meeting. The following Tuesday, April 10, Chris Zheng will present:  
  
Luke O'Connor, Alkes L. Price. [Distinguishing genetic correlation from causation across 52 diseases and complex traits](https://www.biorxiv.org/content/early/2017/10/18/205435). bioRxiv 205435; doi:<https://doi.org/10.1101/205435>

# March 20, 2018

**Presenter**: Zoe Reed

Camelia C. Minica, Conor V. Dolan, Dorret I. Boomsma, Eco de Geus, Michael C. Neale. [Extending Causality Tests With Genetic Instruments: An Integration Of Mendelian Randomization And The Classical Twin Design](https://doi.org/10.1101/134585). bioRxiv 134585.

Next week we'll be back with epigenetics and Lotte Houtepen will be presenting this paper:

Sarah J. Marzi et al. [Analysis of DNA Methylation in Young People: Limited Evidence for an Association Between Victimization Stress and Epigenetic Variation in Blood.](https://www.ncbi.nlm.nih.gov/pubmed/29325449)

Now here is part 9 of the epigeneticist and geneticist saga (part 1-8 [here](https://docs.google.com/document/d/11kXUsNAar4i0oApAMfHZkilucTjR9OsjhAo8H6RaQgs/edit?usp=sharing)):

Although one half of the hijacking team had failed in their pursuit of the epigeneticist, the other half had found a picture resembling the geneticist (almost) perfectly! Without hesitation the team grabbed their kidnapping gear and set-off to find the geneticist, whose twitter feed had also revealed where she worked. Upon arrival in their van outside the workplace, the hijackers setup so they could monitor people coming in and out of the building. Then she appeared. One of the hijackers slid the door open and began jumping out to grab the geneticist. "Wait!", shouted a hijacker in charge of the monitoring. The hijacker noticed something slightly different about her. He couldn't put his finger on it, but they didn't want a repeat of previous failures so the hijackers climbed back into the van. After further reconnaissance work, the hijackers realised that this was in fact the twin sister of the geneticist! Could they get the information they needed from her twin? Or would this additional kidnapping draw unwanted attention? In addition to potentially aiding the hijackers search for the geneticist, twins (studies) may also be used to help address pleiotropy issues in Mendelian randomisation analyses - join us to find out how tomorrow!

# March 13, 2018

**Presenter**: Doretta Caramaschi

Tomorrow morning (10:30-11am in BG7) Doretta Caramaschi will be presenting the following paper:

Tobi EW, Slieker RC, Luijk R, Dekkers KF, Stein AD, Xu KM; Biobank-based Integrative Omics Studies Consortium, Slagboom PE, van Zwet EW, Lumey LH, Heijmans BT. [DNA methylation as a mediator of the association between prenatal adversity and risk factors for metabolic disease in adulthood.](https://www.ncbi.nlm.nih.gov/pubmed/29399631) Sci Adv. 2018 Jan 31;4(1):eaao4364.

If you'd like to read ahead for next week, Zoe Reed will be presenting the following:

Camelia C. Minica, Conor V. Dolan, Dorret I. Boomsma, Eco de Geus, Michael C. Neale. [Extending Causality Tests With Genetic Instruments: An Integration Of Mendelian Randomization And The Classical Twin Design](https://doi.org/10.1101/134585). bioRxiv 134585.

And, finally, the saga of the epigeneticist and geneticist continues. Here is Part 8 (Part 1-7 [here](https://docs.google.com/document/d/11kXUsNAar4i0oApAMfHZkilucTjR9OsjhAo8H6RaQgs/edit?usp=sharing)):

Turns out the hijackers were mistaken about the epigeneticist. The photo they found on the author’s twitter profile did resemble the epigeneticist, but upon further investigation they realised that they had the wrong person. Importantly their epigeneticist had not had any visible body modifications when they had last seen him. In addition, the epigeneticist bore the marks of a somewhat deprived history due to his coming from a poor family and having to support himself through higher education. Compared to the person in the twitter photo (right), his cheek bones were more prominent, his eyes were sadder and cast longer shadows, and his forehead was lined with deep creases. His smile, though, was unmatched. If the hijackers could have compared epigenomes, the differences would have been even more stark. Join the journal club this week to learn more about the epigenetic imprints of early life adversity.

([slides](https://drive.google.com/open?id=1YHQRH2oqcPrRpH6XNcspUURQIGozjvqr))

# March 5, 2018

**Presenter**: Tom Battram

We'll be discussing the following paper tomorrow morning (10:30am, BG7):

Rachel Moore, Francesco Paolo Casale, Marc Jan Bonder, Danilo Horta, BIOS Consortium, Lude Franke, Inês Barroso, Oliver Stegle. A linear mixed model approach to study multivariate gene-environment interactions. bioRxiv 270611; doi: <https://doi.org/10.1101/270611>

Here is part 7 of the ongoing hijacking saga (parts 1-6 are [here](https://docs.google.com/document/d/11kXUsNAar4i0oApAMfHZkilucTjR9OsjhAo8H6RaQgs/edit?usp=sharing)):

Due to the mass twitter hysteria induced within the epigenetics community arising from the realisation DNA methylation may not have as large an impact as previously thought (paper presented last week), the hijackers spotted the epigeneticist on twitter as they couldn't help but get involved in the debate. Through twitter they also learned the original meaning of epigenetics and the frequent misuse of the term so the hijackers decided to ditch any 'epigenetics'-based language to prevent future confusion. Now half the hijacker group started making a plan to catch the epigeneticist and the other half continued trawling the internet in search of the geneticist. Luckily for her the hijackers kept getting distracted by the abundance of interesting genetics papers being posted (including the one being presented tomorrow!)

# February 27, 2018

**Presenter**: Matthew Suderman

We'll be discussing the following paper tomorrow morning (10:30am, BG7). It is likely to have important implications for how we describe and interpret findings in DNA methylation studies.

Ethan Edward Ford, Matthew R. Grimmer, Sabine Stolzenburg, Ozren Bogdanovic, Alex de Mendoza, Peggy J. Farnham, Pilar Blancafort, Ryan Lister

Frequent lack of repressive capacity of promoter DNA methylation identified through genome-wide epigenomic manipulation

bioRxiv 170506; doi: <https://doi.org/10.1101/170506>

([slides](https://drive.google.com/open?id=1py4lwyWR_WQ1-rWCOTNx2xIk2mGykY4n4beRM2aCW9Q))

A re-analysis suggests the opposite: <https://www.biorxiv.org/content/early/2018/08/01/381145>

This paper actually makes an appearance in Part 6 of our ongoing hijacking saga (parts [1-5](https://docs.google.com/document/d/11kXUsNAar4i0oApAMfHZkilucTjR9OsjhAo8H6RaQgs/edit?usp=sharing) are [here](https://docs.google.com/document/d/11kXUsNAar4i0oApAMfHZkilucTjR9OsjhAo8H6RaQgs/edit?usp=sharing)):

Both researchers were relieved to safely return home and hoped that they could put all the hijacker hijinks behind them. The hijackers had a different idea. Knowing only the researcher's faces but not their names, they sought to find them by trolling through images on academic web sites and twitter profiles. Before long, the language of (epi)genetics became so familiar that it began appearing in their everyday language. A loud but irrelevant person was labelled a 'passenger'. New recruits were said to be 'uncanned', possibly a reference to canalisation. Bosses were called 'hubs', enforcers were 'regs', likely short for 'regulators'. Someone good at recruiting new members was 'mitotic'. An operation in action was 'acetylated'. A depressing person was called a 'dmeth'. However, after spotting discussion of our journal club biorxiv paper on twitter, some are suggesting that 'dmeth' may now be passe.

# February 20, 2018

**Presenter**: Ashley Budu-Aggrey

Tomorrow Ashley Budu-Aggrey is presenting the following paper:

Bayesian model comparison for rare variant association studies of multiple phenotypes. DeBoever et al. 2018. Biorxiv  
<https://www.biorxiv.org/content/early/2018/01/31/257162>

Looks really interesting, hope to see you there. Usual time of 10.30–11am in BG7.  
  
Now time for the next exciting instalment of our exciting hijacking saga:  
  
Part 5.  
  
The geneticist and the epigeneticist were on strike, due to some kind of dispute regarding pensions at their respective universities. Everything shut down. Not much happened. There were no interesting happenings that reflected the relative superiority of one of their disciplines over the other’s.

([slides](https://drive.google.com/open?id=1O0sOdII2LOAuH37KOZ-TiRb8NTVUB8op))

# February 13, 2018

**Presenter**: Matthew Suderman

Lu AT, et al. [GWAS of epigenetic aging rates in blood reveals a critical role for TERT](https://www.ncbi.nlm.nih.gov/pubmed/29374233). Nat Commun. 2018 Jan 26;9(1):387.

If you do plan to attend, do check out part 4 of our exciting hijacking saga (Parts 1-3 are below):

Part 4

Needless to say, the hijackers were embarrassed and angry and more determined than ever to find the researchers. One of them had spent a few months in college before being expelled for using the computer network to mine bitcoin. He remembered that professors were often away attending conferences and suggested that they check local conference schedule. Sure enough, a quick internet search turned up an Atlantic Society of Human (Epi)Genetics meeting. After rushing to the venue, the hijackers realised that their task would not be easy, there were 8000 attendees and too many parallel sessions to monitor them all. They decided to select the most likely sessions and assign one to each hijacker. Although the geneticist and epigeneticist were both presenting that day, both avoided attracting the hijackers. The epigeneticist's session was titled "A critical assessment of the genetics of epigenetic aging". Although the title sounded intriguing, the hijackers decided that an expert in *both* genetics and epigenetics would be called something other than simply a geneticist or epigeneticist, perhaps something more like amazeballseticist. The geneticist escaped due to pure random chance: the titles of the genetics sessions were all so similar sounding that the hijackers simply selected a subset uniformly at random.

([slides](https://drive.google.com/open?id=1KQIICWE-CeYmyND5PJnsxXinL9_Qr3Wn0EfKzQ3zSr8))

# February 6, 2018

**Presenter**: Laurence Howe

[Genetic architecture: the shape of the genetic contribution to human traits and disease](https://www.nature.com/articles/nrg.2017.101)

Usual time of 10:30 to 11:00 in BG7.

And now, the saga continues:

Part 3

To thank her rescuer, the next day the geneticist offered to take the epigeneticist to a fancy restaurant for lunch. Whilst the epigeneticist was describing the wonders of transgenerational epigenetic inheritance, the geneticist's mind (for some reason) drifted off and her gaze was caught by the street carnival through the window. Then she noticed three men approaching others with two pieces of paper. A horrible realisation hit the geneticist as they turned around and revealed the papers... It was the hijackers looking for them. A man pointed to the restaurant. The hijackers turned. And for what seemed like a millennium the two groups locked eyes. Then, in a panic the scientists rushed towards the kitchen with the hijackers in close pursuit. They exited through the back entrance, directly onto the street. Both groups entered into the swollen carnival crowd. The hijackers gained on the two scientists, following the geneticists clear red hat. Soon they caught up and tackled their target and quickly tied her up. She turned around. But it wasn't the geneticist... She had tricked the hijackers, who were now surrounded people, infuriated because they missed their opportunity again. The geneticist efficiently lead the scientists through the crowd and to safety. "That was amazing!” exclaimed the epigeneticist. The geneticist replied, "It was nothing, I'm used to navigating large sample sizes.”

# January 30, 2018

**Presenter**: Matthew Suderman

It is epigenetics turn this week and we have two exciting conclusions for you:

1. Join us tomorrow (BG7 at 10:30am) for final discussion of the epigenetic supersimilarity publication we started two weeks ago.   
     
   Van Baak TE, Coarfa C, Dugué PA, Fiorito G, Laritsky E, Baker MS, Kessler NJ, Dong J, Duryea JD, Silver MJ, Saffari A, Prentice AM, Moore SE, Ghantous A, Routledge MN, Gong YY, Herceg Z, Vineis P, Severi G, Hopper JL, Southey MC, Giles GG, Milne RL, Waterland RA. [Epigenetic supersimilarity of monozygotic twin pairs](https://www.ncbi.nlm.nih.gov/pubmed/29310692). Genome Biol. 2018 Jan 9;19(1):2.

And now, the moment you didn't know you'd been waiting for, the exciting conclusion of Gib's hijacking tale:

Part 2

As the geneticist hurtled toward the ground, the epigeneticist frantically glanced about the cabin and noticed that each hijacker was wearing a parachute. In a single deft movement, he grabbed one and flung his body out of the plane. The owner of the parachute instinctively grabbed at the door frame with one hand and with the other released the buckle of his parachute. Instantly the epigeneticist was free and hurtling through the air downward. He slipped on the parachute and dove toward the earth hoping to catch up to the geneticist. The geneticist, no longer so eager to die, was now frantically clawing at the air. This slowed her descent just enough so that seconds later the epigeneticist was able to latch on to one of her wrists, strap their bodies together, and then release the parachute. Gasping for air as they lay on the ground, the geneticist whispered, "You - saved - my - life! How will I - ever - thank you". The epigeneticist smiled grimly and replied, "Think nothing of it. Years ago I would have never even attempted such a dangerous rescue, but the years of scepticism and ridicule that I endured before epigenetics became popular changed me. Each crushing review directed at my work forced me to face my worst fears and over time, by some mysterious mechanism, I gained confidence.

# January 23, 2018

**Presenter**: Gibran Hemani

A geneticist and an epigeneticist were sitting on a plane. Suddenly, hijackers took control of the cabin and took the two scientists captive. They said, “We are going kill one of you. We will decide who gets to live by evaluating which of you does the most interesting research”.

Each of the scientists was given an hour to describe their respective disciplines. The geneticist went first, and narrated the exciting history of her field, describing how the transmission of genetic material reconciled the paradox of natural selection with genetic diversity, the discovery of the DNA molecule, and how this gave rise to fascinating insights into evolution and disease. She concluded that biology is nothing more and nothing less than genetics.

The hijackers were moved to tears, they hooted and applauded. Then they turned to the epigeneticist and said, “Ok, your turn”.

The epigeneticist stood up and began, “I will now give a brief presentation on epigenetics”. At this, the geneticist stood up, and screamed “Oh god I can’t bear to sit through another one of these”, and promptly flung herself out of the plane to her certain death.

**tl;dr** Genetics is back on the (epi)genetics journal club agenda! And from now on we’ll alternate the weeks between epigenetics and genetics. Tomorrow (Tuesday 23 Jan) I will present:

[Bayesian analysis of genetic association across tree-structured routine healthcare data in the UK Biobank. Cortes et al. Nature Genetics 49, 1311–1318 (2017).](https://www.nature.com/articles/ng.3926)

# January 16, 2018

**Presenter**: Matthew Suderman

Monozygotic twins, two almost identical human beings. How cool is that? If you're thinking of producing a pair, however, it's worth carefully considering the pros and cons.

Some of the cons for parents include [increased stress](https://www.ncbi.nlm.nih.gov/pubmed/23541543), [greater risk of divorce](https://www.ncbi.nlm.nih.gov/pubmed/21422862), [increased anxiety possibly delaying child mental development](https://www.ncbi.nlm.nih.gov/pubmed/17228752), [decreased parent-child interaction resulting in delayed language development](https://www.ncbi.nlm.nih.gov/pubmed/12635965), and [increased risk of depression](https://www.ncbi.nlm.nih.gov/pubmed/2025725). Wow, sounds tough.

Some notable pros include increased upper body strength, double tax deduction, well more than double the attention, [increased life-span](https://www.ncbi.nlm.nih.gov/pubmed/21561975), and, last but certainly not least, the opportunity to conduct one’s very own private study of environment and human development (kind of like these [folk](https://www.huffingtonpost.com/alex-boese/a-brief-history-of-scientists-experimenting-on-their-own-kids_b_1840029.html) and more recently [these](http://www.nytimes.com/2009/01/18/science/18kids.html), but maybe not like this [guy](https://en.wikipedia.org/wiki/Melvin_L._Morse)).

Tomorrow morning (BG7, 10:30am), we will discuss the following paper showing that monozygotic twins may be even more similar than genetic similarity would imply:

Van Baak TE, Coarfa C, Dugué PA, Fiorito G, Laritsky E, Baker MS, Kessler NJ, Dong J, Duryea JD, Silver MJ, Saffari A, Prentice AM, Moore SE, Ghantous A, Routledge MN, Gong YY, Herceg Z, Vineis P, Severi G, Hopper JL, Southey MC, Giles GG, Milne RL, Waterland RA. [Epigenetic supersimilarity of monozygotic twin pairs](https://www.ncbi.nlm.nih.gov/pubmed/29310692). Genome Biol. 2018 Jan 9;19(1):2.

([slides](https://drive.google.com/open?id=1Kez3lqIRATdTZPoCzmCH073BnW8QSk7wPdGzy6d-P5s))

# January 9, 2018

**Presenter**: Luisa Zuccolo

**Special session 10:30-12 on phenome-wide association studies.**

Polimanti R, Kranzler HR, Gelernter J. [Phenome-Wide Association Study for Alcohol and Nicotine Risk Alleles in 26394 Women](https://www.ncbi.nlm.nih.gov/pubmed/27187070). Neuropsychopharmacology. 2016 Oct;41(11):2688-96.

From Luisa:

“As a one-off session with different format from usual, I suggest to spend longer examining the study and discussing different aspects (technical choices, interpretation, relevance for our research in IEU etc). It will be pitched at a more basic level than current journal club, thanks to dedicating longer time to it. I am hoping 1st and 2nd year phd students will feel welcome to attend and ask any questions - we should have enough time to answer those. Or anyone else with an interest (but little experience) in PheWAS.”

# December 19, 2017

**Presenter**: Matthew Suderman

Growing tired of having to assemble ever larger populations for genome- and epigenome-wide association studies just so you can identify a few more associated loci or tweak estimates of variance explained? Fed up with hundreds of co-authors trying to move closer to the coveted first or last positions on your paper?

Well, you don't have to any more and you can still publish in the big journals on your favourite topic. Take for example, major depressive disorder (MDD). The [largest MDD GWAS](https://www.biorxiv.org/content/early/2017/07/24/167577) used 130K cases and 330K controls to identify 44 loci and increase SNP-heritability to about 9%. Compare that to a [recent publication](https://www.ncbi.nlm.nih.gov/pubmed/28825715) describing a transcriptome-wide association study of MDD published in Nature Medicine (IF 29). This study included only 48 participants ... yes 48. That is likely fewer than the number of co-authors on your last publication. Of course it did help that the participants were no longer alive, that several brain regions were analysed, that findings compared favourably to a mouse model ... but still 48.

Join us tomorrow at 10:30am in BG7 to hear more:

Labonté B, et al. [Sex-specific transcriptional signatures in human depression](https://www.ncbi.nlm.nih.gov/pubmed/28825715). Nat Med. 2017 Sep;23(9):1102-1111.

([slides](https://drive.google.com/open?id=1MpTEbEK4u_aEa7Pem1Q8QWzmi7mLzYWMZiYsCt8up7E))

# December 12, 2017

**Presenter**: Matthew Suderman

Some of us have just gotten used to the term '[bump hunter](https://www.google.co.uk/url?sa=t&rct=j&q=&esrc=s&source=web&cd=3&cad=rja&uact=8&ved=0ahUKEwjn9cnQqP_XAhXpCsAKHZP_D9IQFgg0MAI&url=https%3A%2F%2Fwww.ncbi.nlm.nih.gov%2Fpubmed%2F22422453&usg=AOvVaw0sSn5jXFDChhaaspYyoUNG)', and now we have '[gap hunter](https://epigeneticsandchromatin.biomedcentral.com/articles/10.1186/s13072-016-0107-z)'. Well, there are apparently two kinds of gap hunters of interest to us (if you

are into [racing drones](https://www.youtube.com/watch?v=vClsGScB84U), then there are three):

1. Business guru and self-described gap hunter [Nigel Collin](http://www.gameofinches.com.au/) believes that the biggest gap in the IEU is our inability to find gaps. If only we could become gap hunters instead of idea hunters, then “unique and potentially lucrative opportunities would present themselves”. To help us, he has created [Gap Hunter](http://www.gameofinches.com.au/the-gap-hunter), "a program designed to find gaps within your organisation that if acted upon will boost your bottom line." He guarantees that it will find at least three so what are we waiting for?!
2. Gap hunting is a data-driven alternative to the common practice of excluding all probes in an Illumina Methylation BeadChip dataset that might be impaired by common genetic variants. Gap hunting attempts to identify problematic probes by their tell-tail clustered intensity distributions.

Tomorrow morning (10:30am in BG7), we will discuss the second kind of gap hunting:

Andrews SV, Ladd-Acosta C, Feinberg AP, Hansen KD, Fallin MD. ["Gap hunting" to characterize clustered probe signals in Illumina methylation array data](https://www.ncbi.nlm.nih.gov/pubmed/27980682). Epigenetics & Chromatin. 2016 Dec 7;9:56.

([slides](https://drive.google.com/open?id=1FviYidGVaQklk1gpeBphqV0Bg17j4qkkM-Xt49lazrQ))

# December 5, 2017

**Presenter**: Matthew Suderman

Genetic ancestry testing has reached white nationalists and their responses to unfavourable test results have been the topic of academic study (<https://osf.io/preprints/socarxiv/7f9bc>). Below is a representative sample:

1. "When you look in the mirror, do you see a Jew? If not, you’re good"
2. "I think 23andMe might be a covert operation to get DNA the Jews could then use to create bio-weapons for use against us."
3. "You are simply related to some white fool who left some of his DNA with the locals in what is now Senegal."
4. "So in one [white] nation having Ghengis Khan as your ancestor won’t disqualify you, while in others it might."
5. "The reason why I'm more liberal with autosomal DNA is that non-White autosomal DNA can be cut in half every generation from 25,12.5, 6, 3, 1.5, .75 and so on to the point where the non-White admixture is irrelevant."
6. "I do see your 'washing out' of autosomes reasoning, but I also see long-term admixture of those genes more problematic. Once that admixture begins in a population it just builds and builds until you have Brazil."

Tomorrow morning (10:30am in BG7) we will compare Genetic to Epigenetic ancestry testing and discuss the anticipated white nationalist responses to an environmentally responsive genome.

Rahmani E, et al. [Genome-wide methylation data mirror ancestry information.](https://www.ncbi.nlm.nih.gov/pubmed/28149326) Epigenetics Chromatin. 2017 Jan 3;10:1.

([slides](https://drive.google.com/open?id=1ZM6HcCWZ22arbqA702iPPbHCaUGWwdRqmrVMW5RFDiU))

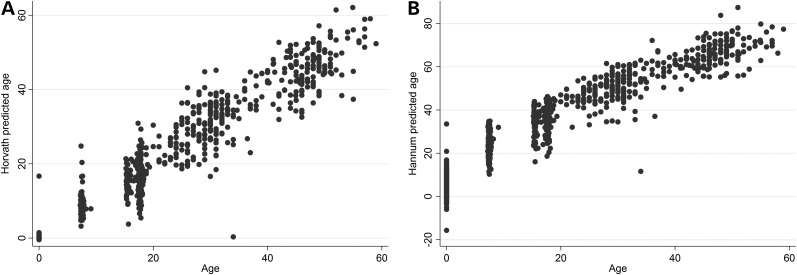
# November 28, 2017

**Presenter**: Matthew Suderman

It is time to get your DNA methylation in order. Insurance company [GWG Life](https://www.gwglife.com/) has begun collecting saliva samples from applicants and has hired Brian Chen as its chief scientific officer. Brian was lead author of [a recent study](https://www.ncbi.nlm.nih.gov/pubmed/27690265) showing associations between DNA methylation and all-cause mortality independent of traditional risk factors.

Some of us have a lot to be worried about. Below are scatterplots comparing DNA methylation age estimates and chronological age in ALSPAC participants. Interesting how some of the infants have age estimates higher than 20 years and at least one 35 year old who appears by one estimate to be an infant and another estimate to be a teen.

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4690495/>

[](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4690495/)

Tomorrow morning (BG7 at 10:30am), we'll be looking at another DNA methylation clock for estimating mitotic age. It was designed differently from previous clocks and is predictive of cancer survival when applied to tumor samples.

Youn A, Wang S. [The MiAge Calculator: a DNA methylation-based mitotic age calculator of Human tissue types](https://www.ncbi.nlm.nih.gov/pubmed/29160179). Epigenetics. 2017 Nov 21:1-42.

([slides](https://drive.google.com/open?id=1dJu4Xv0SvOCdCrHJomgtaEA1eeSjgU0JWuQu2fZTt7o))

# November 21, 2017

**Presenter**: Matthew Suderman

Hidden inside an abandoned Soviet-era bunker, Gena of Warped Cranium hatched a cunning plan to use Open Science to become rich. She would download all genomes she could get her grasping little fingers on and use them to synthesise fragments of DNA. She would call the result Anti-Forensics Powder and sell sachets of it at a premium on the Dark Web.

Before long, Gena was awash with cash and law enforcement baffled by more and more crime scenes contaminated with DNA from thousands of different people. It wasn't long before the Dazzling Eppie read about the mystery from her perch in the Ivory Tower. Between sips of dark brew, she suddenly paused, "I wonder what DNA methylation patterns can be found on that DNA?" To the surprise of all but Eppie, only a few genomes at each crime scene were methylated, those of the criminals and victims.

If you want to be like Eppie and not like Gena, join us for journal club tomorrow morning (BG7, 10:30am). This will be our second session discussing the following publication:

Hannon E, Weedon M, Bray N, O'Donovan M, Mill J. [Pleiotropic Effects of Trait-Associated Genetic Variation on DNA Methylation: Utility for Refining GWAS Loci](https://www.ncbi.nlm.nih.gov/pubmed/28528868). Am J Hum Genet. 2017 Jun 1;100(6):954-959.

([slides](https://drive.google.com/open?id=1rmIIANr_oRKBXaR_mtQCOiQgXoqlvojnLZB7OoVYwN8))

# November 14, 2017

No meeting this week as many of us will be at the [Epigenomics of Common Diseases](https://coursesandconferences.wellcomegenomecampus.org/events/item.aspx?e=638) conference this week.

That said ... So a theatre director, a composer, an author and a scientist walk into a radio studio. No, really, they did this morning and the scientist was our very own Caroline Relton who was interviewed by Francine Stock on [BBC Radio 4](http://www.bbc.co.uk/programmes/b09drjb7) (replay here <http://www.bbc.co.uk/programmes/b09drjb7>). Her interview is about 10 minutes and starts at 23:42. In that short time she introduced epigenetics and epidemiology with the use of helpful analogies as well as references to the composer's play and the author's book while clearing up misconceptions about transgenerational epigenetic inheritance and differentiating between inference in populations and individuals. Author Darren McGarvey liked what he heard and summarised: "the choices that I'm making now could upgrade the family DNA to some extent".

# November 7, 2017

**Presenter**: Matthew Suderman

Everyone has them   
but no two have the same  
and no one can have more than a few.  
They often create controversy.  
The saying 'actions speak louder than words' certainly applies.  
Being choked typically changes them.  
   
Tomorrow morning (Tuesday, 10:30am in BG7), we will attempt to behave like mature adults by discussing setting priorities, specifically an approach for prioritizing genes using DNA methylation and gene expression:  
   
Hannon E, Weedon M, Bray N, O'Donovan M, Mill J. [Pleiotropic Effects of Trait-Associated Genetic Variation on DNA Methylation: Utility for Refining GWAS Loci](https://www.ncbi.nlm.nih.gov/pubmed/28528868). Am J Hum Genet. 2017 Jun 1;100(6):954-959.

([slides](https://drive.google.com/open?id=1rmIIANr_oRKBXaR_mtQCOiQgXoqlvojnLZB7OoVYwN8))

# October 30, 2017

**Presenter**: Matthew Suderman

Acharya CR, Owzar K, Allen AS. [Mapping eQTL by leveraging multiple tissues and DNA methylation.](https://www.ncbi.nlm.nih.gov/pubmed/29047346) BMC Bioinformatics. 2017 Oct 18;18(1):455.

Tomorrow morning (10:30am in BG7) we will be leveraging multi-tissue epigenomic profiles to exploit synergistic relationships between omic profiles with the aim of growing our grasp of gene regulatory mechanisms using an out of the box paradigm that admittedly pushes the envelope but is holistic and therefore bound to bring about a sea change to really allow bioinformatic deep learning applied to big omic data to do some long-due heavy lifting, it will be a clear win-win.

Acharya CR, Owzar K, Allen AS. [Mapping eQTL by leveraging multiple tissues and DNA methylation.](https://www.ncbi.nlm.nih.gov/pubmed/29047346) BMC Bioinformatics. 2017 Oct 18;18(1):455.

Does that leave you buzzing? Send me your favourite omics buzzword and we'll play some [buzzword bingo](https://en.wikipedia.org/wiki/Buzzword_bingo)!



DILBERT © 1994 Scott Adams.

Still trying to work out the monkey's age from last week, [here](https://docs.google.com/a/bristol.ac.uk/document/d/19e3Tt0LfdfGoL5GW4BCAvOcOaGsWUeY8Aii9n3bqqiY/edit?usp=sharing) is one solution.

([slides](https://drive.google.com/open?id=1rfDZVNW-fIJlcAQlTGPBi3r72uY3JGzfJRPOGJQUez0))

# October 24, 2017

**Presenter**: Matthew Suderman

See if you can determine the age of this monkey ([source](http://www.sas.rochester.edu/phl/puzzles.html)):

“The sum of the ages of the monkey and its mother is eight years .... The mother is twice as old as the monkey was when the mother was half as old as the monkey will be when the monkey is three times as old as its mother was when she was three times as old as the monkey was.”

Yes, the age can be calculated, although it may have been easier for some to have just taken a saliva sample from the monkey and measure microRNA or mRNA expression or DNA methylation. Each of these approaches would give a slightly different answer but on average they should all be pretty close:

Huan T, Chen G, Liu C, Bhattacharya A, Rong J, Chen BH, Seshadri S, Tanriverdi K, Freedman JE, Larson MG, Murabito JM, Levy D. [Age-associated microRNA expression in human peripheral blood is associated with all-cause mortality and age-related traits](https://www.ncbi.nlm.nih.gov/pubmed/29044988). Aging Cell. 2017 Oct 17.

([slides](https://drive.google.com/open?id=1kWo1SA14TN9LCB8h2WP-MhtpjuYAMC_ezI9f9lMLTzA))

# October 17, 2017

**Presenter**: Matthew Suderman

For too long epigenetics has suffered as the less loved and often despised younger sibling of genetics. Even its name contains 'genetics', as if it were a mere speciality subsumed by it. No methylomic association no matter how strong is ever safe from disparaging allegations of reverse causality or technical artefact until mendelian randomization has had its say. The arbiter can be the lowliest geneticist, or even an economist, as if the beauty and intricacy of the biological can be boiled down by basic mathematics to a mere genetic variant. Tomorrow we will discuss something truly insidious, genetic signal masquerading as an exposure effect, making non-smokers appear as smokers. The innocent looking genetic variant cannot be trusted after all!

Gao X, Thomsen H, Zhang Y, Breitling LP, Brenner H. [The impact of methylation quantitative trait loci (mQTLs) on active smoking-related DNA methylation changes](https://www.ncbi.nlm.nih.gov/pubmed/28824732). Clin Epigenetics. 2017 Aug 17;9:87. doi: 10.1186/s13148-017-0387-6. eCollection 2017.

([slides](https://drive.google.com/open?id=13Wr1jrzwcewNTfD6QBMkxtsE8hDF-W_Qj5EQZ3busW8))

# October 3, 2017

**Presenter**: Charleen Adams

Our paper this week will be presented by Charleen Adams (Tuesday, 10:30am in BG7). She will present evidence that DNA methylation patterns played an key role in determining which genomic regions were available for sequence changes during primate evolution.

Fukuda K, Inoguchi Y, Ichiyanagi K, Ichiyanagi T, Go Y, Nagano M, Yanagawa Y, Takaesu N, Ohkawa Y, Imai H, Sasaki H. [Evolution of the sperm methylome of primates is associated with retrotransposon insertions and genome instability](https://www.ncbi.nlm.nih.gov/pubmed/28637190). Hum Mol Genet. 2017 Sep 15;26(18):3508-3519.

Given the intimate role that epigenetic mechanisms have played in our biological history, I thought it appropriate to reproduce below the lyrics of a #1 hit by the rock band Extreme.

More than DNA

by Extreme

Seeing TATAAA

Is not the only thing I want to find in you

It's not that I want you

Untranscribed, but if you only knew

How easy it would be to know where to anneal

More than bases is what you need to show to make it real

With chromatin you wouldn't have to say where is TATAAA

'Cause I'd already know

What would you do if a novel variant was needed from you

An alternate start site to repeal

And a novel transcript to unseal

Selection too slow to mutate sequence the right way

We'd quickly generate something new

Just by having demethylated you.

From Charleen:

After giving it several tight reads, I would not claim that their paper points to a causal relationship between methylation and evolution. The authors even provide this cautionary statement: “Although it is tempting to speculate that the human-specific sperm HMDs [hypomethylated domains] is involved in CNV formation, establishment of the causal relationship awaits future studies.”  
   
The bulk of what they present points to the primacy of genetic change on methylation—not the other way around. And not just in this paper, but in their previous paper on methylation and transcription factor binding sites (TFBSs). Here’s what they wrote about their previous finding. Notice the direction of causality (my emphasis): “This suggested that inter-species epigenetic differences can arise via genetic differences in transcription factor bindings sites.”  
   
Moreover, the stated justification for examining the relationship between retrotransposons and methylation is that “retrotransposon insertation or deletion can cause local epigenetic change”… And, they conclude that “de novo SVA insertions generate epigenetic variations within the human population.”  
   
The authors conclude that genetic changes in TFBSs and retrotransposon insertions are associated with changes in the primate methylome and speculate that the HMDs may prime the genome for instability, something that is NOT tested in their work here but suggested by the association of copy number variants with HMDs in sperm.  
   
Thus their provocative title is a bit misleading—and in contradiction with both their own caution against causal inference and the associative rather than experimental nature of their study.

([slides](https://drive.google.com/open?id=0B-peG00QorQjY3d1Z3hwMzhSSkE))

# September 26, 2017

**Presenter**: Matthew Suderman

In a contest of wits, it might be unwise to bet against the fish according to Jonathan Balcombe, author of '[What a fish knows](https://www.scientificamerican.com/store/books/what-a-fish-knows-the-inner-lives-of-our-underwater-cousins/)'. This is particularly true if it is from the 'Molly' family. The [Amazon Molly](https://en.wikipedia.org/wiki/Amazon_molly) for example has managed to produce viable embryos using two maternal genomes. The [Amazon Molly](https://en.wikipedia.org/wiki/Amazon_molly) is in fact so good at this that is has almost entirely dispensed with any need for males. It produces offspring, always female, by mating with males of other species such as the [Atlantic Molly](https://en.wikipedia.org/wiki/Poecilia_mexicana) and then ditching the male genetic material. The [Atlantic Molly](https://en.wikipedia.org/wiki/Poecilia_mexicana) male obliges because he knows that being seen with an Amazon Molly will drive his real interest, Atlantic females, into a jealous frenzy. And his schemes don't end there. He has been known to feign attraction for one female in order to distract rivals from his preferred female.

We humans are also pretty clever. We've created mammalian embryos with two maternal genomes to learn more about [genomic imprinting](https://en.wikipedia.org/wiki/Genomic_imprinting). Pretty good for bunch of non-fish! Unfortunately, unlike Molly embryos, these do not survive for more than a few days. Tomorrow morning (10:30am in BG7) we will discuss how they were recently used to discover a new role for H3K27me3 in controlling genomic imprinting:

Inoue A, Jiang L, Lu F, Suzuki T, Zhang Y. [Maternal H3K27me3 controls DNA methylation-independent imprinting](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Abstract&list_uids=28723896). Nature. 2017;547(7664):419–24.

Hanna CW, Kelsey G. [Genomic imprinting beyond DNA methylation: a role for maternal histones](https://www.ncbi.nlm.nih.gov/pubmed/28927436). Genome Biol. 2017 Sep 19;18(1):177.

# September 19, 2017

**Presenter**: Matthew Suderman

Predicting the success of a sequel to a film (or MRC IEU unit) can be difficult. Some very intelligent people make sequels every year that flop and receive a [Golden Raspberry Award](https://en.wikipedia.org/wiki/Golden_Raspberry_Award_for_Worst_Prequel,_Remake,_Rip-off_or_Sequel) for their efforts.

Fortunately a few academics believe that they have discovered the surprising ingredients for sequel success. For example, [audience attendance](https://doi.org/10.1109/ICMSE.2013.6586370) but not critical response or commercial success of the original film is predictive. In the sequel itself, it is essential to have [star continuity and to have conceived of a multi-film story right from the beginning](https://doi.org/10.1509/jmkg.73.6.167).

These findings suggest that IEU 2.0 success will depend not on reviewer comments or how much funding we have received to date but on how often we've been quoted in newspapers, the number of star researchers we have retained, and that we continue to follow the twists and turns laid out in our unit guide, George's Little MR Book.

And as for the journal club, we decided on a sequel with last weeks paper. Raspberries welcome.

Ng B, White CC, Klein HU, Sieberts SK, McCabe C, Patrick E, Xu J, Yu L, Gaiteri C, Bennett DA, Mostafavi S, De Jager PL. [An xQTL map integrates the genetic architecture of the human brain's transcriptome and epigenome.](https://www.ncbi.nlm.nih.gov/pubmed/28869584) Nat Neurosci. 2017 Sep 4. doi: 10.1038/nn.4632.



[slides](https://drive.google.com/open?id=1-PcCVd1EQcp6X5N9dVUMwI0T7I0k0peBnuhOXjG5ZHs)

# September 12, 2017

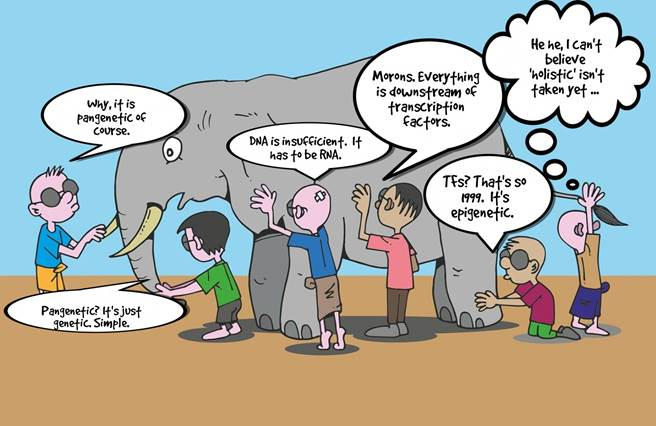
**Presenter**: Matthew Suderman

Tomorrow morning (Tuesday Sept 12, 10:30am in BG7), we will discuss an effort to integrate genomic, transcriptomic and epigenomic profiles of human brains.

Ng B, White CC, Klein HU, Sieberts SK, McCabe C, Patrick E, Xu J, Yu L, Gaiteri C, Bennett DA, Mostafavi S, De Jager PL.

[An xQTL map integrates the genetic architecture of the human brain's transcriptome and epigenome.](https://www.ncbi.nlm.nih.gov/pubmed/28869584) Nat Neurosci. 2017 Sep 4.

The discussion will cover both the practical and philosophical. On the practical side, we will ask about the utility of such an integration (i.e. will it help me publish more papers). On the philosophical side, we will discuss whether or not we have finally arrived at that auspicious moment in history when we can finally and truly say: "we have all been right, it's an elephant."



(credits to [https://phraseit.net](https://phraseit.net/), <https://pixabay.com/en/blind-men-elephant-story-feel-see-1458438/>, and me)

[slides](https://drive.google.com/open?id=1-PcCVd1EQcp6X5N9dVUMwI0T7I0k0peBnuhOXjG5ZHs)

# September 5, 2017

**Presenter**: Matthew Suderman

Tenacious like an ancient curse, the (epi)genetics journal club is back.

As you know, curses typically run in families.

"You shall not worship them or serve them; for I, the LORD your God, am a jealous God, visiting the iniquity of the fathers on the children, on the third and the fourth generations of those who hate Me,

- The Bible (Exodus 20:5)

There are many examples:

- [curse of Atreus](https://en.wikipedia.org/wiki/Atreus) resolved by having Orestes kill his mother (wonder it works in general, to undo curses by killing ancestors).

- [curse of Mysore Wadiyar dynasty](https://en.wikipedia.org/wiki/Wadiyar_dynasty#Curse_on_Wadiyars) to never beget children (mysteriously effective though only for every second generation).

- many [recent examples](http://crimeviral.com/2016/03/12-famous-families-who-were-tragically-cursed/) including the [Guiness](http://www.independent.ie/opinion/editorial/the-black-curse-strikes-guinness-dynasty-again-26209416.html), [Kennedy](https://en.wikipedia.org/wiki/Kennedy_curse) and [Von Erich](https://en.wikipedia.org/wiki/Von_Erich_family) family curses.

- a charming band called "[The family curse](http://www.frcollective.com/the-family-curse.html)" appears to suffer from exactly that according to my daughter.

Fortunately, science has discovered the mechanism behind family curses: epigenetics. Since epigenetic changes are reversible, so are family curses.

[Order instructional videos now](https://vimeo.com/97876005)!

Tomorrow morning we'll discuss evidence for DNA methylation biomarkers of grandmaternal stress:

Serpeloni F, Radtke K, de Assis SG, Henning F, Nätt D, Elbert T.

[Grandmaternal stress during pregnancy and DNA methylation of the third generation: an epigenome-wide association study.](https://www.ncbi.nlm.nih.gov/pubmed/28809857)

Transl Psychiatry. 2017 Aug 15;7(8):e1202. doi: 10.1038/tp.2017.153.

PMID: 28809857

I did check, and the associations do not appear to be driven by cigarette smoking (either own or prenatal).

[slides](https://drive.google.com/open?id=1szqjOYEAMWul0yk_sRIUPfK34zwTA8CpN_SKZvuQbv4)

# August 1, 2017

**Presenter:** Lotte Houtepen

I've spent the last week in my hometown and come across all sorts of objects and places that bring back vivid memories:

* the small orange wooden chair on which I split open my forehead,
* the school into which we crashed my model plane on its very first flight,
* the tree out of which I shot a crow with my slingshot,
* the building site where I fell off the scaffolding,
* the church where I felt a sudden panic the evening before getting married.

Although these triggered memories include details that I thought were long forgotten, I don't experience them as if they are happening all over again. People who develop PTSD following a traumatic experience are not so fortunate, recalling the experience can be just as terrifying and mentally damaging.

Tomorrow morning (10:30am in BG7), Lotte Houtepen will present a paper describing how DNA methylation changes in individuals who experience trauma and it differs in those who go on to develop PTSD.

Rutten et al. [Longitudinal analyses of the DNA methylome in deployed military servicemen identify susceptibility loci for post-traumatic stress disorder](https://www.ncbi.nlm.nih.gov/pubmed/28630453). Mol Psychiatry. 2017 Jun 20.

# July 25, 2017

**Presenter:** Tom Richardson

Ticklishness has apparently been localised to neuronal activity in the deep layers of the somatosensory cortex ([ref](http://science.sciencemag.org/cgi/doi/10.1126/science.aah5114)). However, if you are a fan of tickling, do not worry, your fun has not been simply reduced to the flow of neurotransmitters between a few neurons. The authors of this study also show that the neuronal response of this brain region is linked to play behaviour and can be modulated by mood. For example, they show that the tickle response can be suppressed by anxiety. This is possibly the reason why it's not a good idea to try to tickle a stranger. But make a rat feel safe and they apparently love to be tickled, will squeal with delight and beg for more: <https://youtu.be/d-84UJpYFRM?t=53>.

Given these findings, ticklishness should probably be considered a complex trait so, as Tom Richardson will show tomorrow morning (10:30am in BG7), we should expect the genetic variants influencing ticklishness to be scattered across the genome affecting a large number of genes belonging to a variety of pathways. In fact, we should expect that "most heritability" of such a complex trait will be "explained by effects on genes *outside* core pathways".

Boyle EA, Li YI, Pritchard JK.

[An Expanded View of Complex Traits: From Polygenic to Omnigenic.](https://www.ncbi.nlm.nih.gov/pubmed/28622505)

Cell. 2017 Jun 15;169(7):1177-1186. doi: 10.1016/j.cell.2017.05.038.

# July 18, 2017

**Presenter:** Doretta Caramaschi

A lot things parents say are not true, e.g.

1. this is going to hurt me more than it hurts you
2. if you eat your [boogers](https://www.youtube.com/watch?v=BBw1GWsr8mI), worms will grow in your stomach
3. keeping secrets will make you sick
4. the ice cream truck plays music only when the ice cream is all gone
5. you're thirsty? would you like some sky juice?
6. if you are sad, they'll have to give you a sad meal

In fact, an over-simplified explanation for "educational purposes" is often called a [lie-to-children](https://en.wikipedia.org/wiki/Lie-to-children).

However, when your parent accused you of "doing my head in", they were possibly telling the truth. The many ways that you disrupted their sleep, from your incessant crying as an infant to the police calling to have you picked up at 2am, [likely increased their risk of Alzheimer's disease](http://www.neurology.org/content/early/2017/07/05/WNL.0000000000004189).

Tomorrow morning (10:30am in **OS6**), Doretta Caramaschi will present a paper describing how epigenetic processes may play a role in the link between disrupted diurnal and seasonal rhythms and Alzheimer's disease risk.

Lim AS, Klein HU, Yu L, Chibnik LB, Ali S, Xu J, Bennett DA, De Jager PL. [Diurnal and seasonal molecular rhythms in human neocortex and their relation to Alzheimer's disease](https://www.ncbi.nlm.nih.gov/pubmed/28368004). Nat Commun. 2017 Apr 3;8:14931.

# July 4, 2017

**Presenter:** Esther Walton

A conversation overheard somewhere in an epigeneticists dream world:

"Our son has", she spelled it in a whisper, "A-D-H-D."

"What?!" he asked loudly drawing surprised glances from around the room.

She wrote it down.

Lowering his voice he asked, "But how? Neither of us ..."

"It's not genetic," she interrupted impatiently, "and this never would have happened if you had actually completed your preconception intervention treatments."

"But", he protested, "I did complete them, although I was never sure what spending time with elderly people had to do with me passing on ADHD to our son."

"It's science, we can't expect to always understand. The doctor checked your epigenome and saw no changes related to ADHD, although she did see significant age acceleration."

"That's not surprising given who I was spending time with", he concluded. "But it wasn't all bad. For once, at the Adult Disability and Health Care centre, I could actually hear what people were saying."

Tomorrow morning (10:30am, BG7), Esther Walton will be discussing a follow-up to her [recent](https://www.ncbi.nlm.nih.gov/pubmed/27217153/) analysis of ADHD symptoms and DNA methylation.

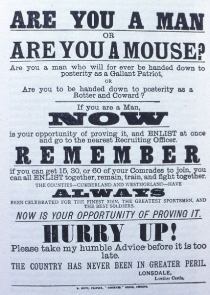
Heinrich H, Grunitz J, Stonawski V, Frey S, Wahl S, Albrecht B, Goecke TW, Beckmann MW, Kornhuber J, Fasching PA, Moll GH, Eichler A.

[Attention, cognitive control and motivation in ADHD: Linking event-related brain potentials and DNA methylation patterns in boys at early school age.](https://www.ncbi.nlm.nih.gov/pubmed/28630479)

Sci Rep. 2017 Jun 19;7(1):3823

# June 27, 2017

**Presenter:** Matthew Suderman



We humans have apparently been disparaging mice for [for centuries](https://english.stackexchange.com/questions/322561/are-you-a-man-or-a-mouse-phrase-origin). One notable exception was the unhappily married Mr Peck who at times wished that he could have been a mouse:

MRS. PECK (contemptuously): "What are you, anyhow, a man or a mouse?"

MR. PECK (bitterly): "A man, my dear. If I were a mouse I'd have you up on that table yelling for help right now." ([link](https://books.google.co.uk/books?id=MrI5AQAAMAAJ&pg=PA725&dq=%22man+or+a+mouse%22&hl=en&sa=X&redir_esc=y#v=onepage&q=%22man%20or%20a%20mouse%22&f=false))

Robert Burns also [envied the mouse for neither regretting the past nor being anxious for the future](https://en.wikipedia.org/wiki/To_a_Mouse).

Whether or not Burns was right, mouse DNA methylation does record the passing of time. In journal club this week (10:30am, **BG10 this week**), we will compare DNA methylation age estimates in mouse and human and see what we can learn from the mouse.

Wagner W. [Epigenetic aging clocks in mice and men.](https://www.ncbi.nlm.nih.gov/pubmed/28615041) Genome Biol. 2017 Jun 14;18(1):107.

([slides](https://drive.google.com/open?id=15d9XOI-wd9EkgdBzigRaiYbBY71MoGy8C8lvMkUUMBE))

# June 20, 2017

There will be no (epi)genetic journal club tomorrow as several of us will be away for a meeting.

In the meantime, I'd like to highlight one of the oddest epigenetics results in quite a while (and that's saying a lot coming from epigenetics).

By now "CpG" appears so commonly in text and speech that it practically has word status. But what about "GpC", it's awkward-sounding sibling? Experimental data suggests that the mitochondrial world might prefer to the GpC methylation:

van der Wijst MG, van Tilburg AY, Ruiters MH, Rots MG.

[Experimental mitochondria-targeted DNA methylation identifies GpC methylation, not CpG methylation, as potential regulator of mitochondrial gene expression.](https://www.ncbi.nlm.nih.gov/pubmed/28282966)

Sci Rep. 2017 Dec;7(1):177.

# June 13, 2017

**Presenter:** James Staley

Tomorrow morning (BG7, 10:30am), James Staley will describe a large-scale blood plasma **protein-QTL** analysis and explain how the results can be used to inform drug development:

Sun, et al. [Consequences Of Natural Perturbations In The Human Plasma Proteome](http://biorxiv.org/content/early/2017/05/05/134551). bioRxiv 134551; doi: <https://doi.org/10.1101/134551>

We can learn a lot from this paper, not only from its high impact contents, but also by how it is written. In particular, consider the title. By including the words "natural perturbations", the authors have linked their paper to a highly controversial topic, climate change, potentially leading to thousands of positive citations like the following: "It's just a natural perturbation [Sun et al. bioRxiv 2017]".

You might be surprised to learn that there are in fact many ways to increase the citation frequency of your paper (33 to be exact):

Ebrahim, et al. [Effective Strategies for Increasing Citation Frequency](http://www.ccsenet.org/journal/index.php/ies/article/view/30366). International Education Studies Vol. 6, No. 11, November 2013

I am working very hard to utilise strategy #21: make sure that your paper is rejected by at least one journal.

# June 6, 2017

Due to the Epigenetic Epidemiology short course this week, journal club is cancelled. We'll resume next week as usual.

In the meantime, if you experience any symptoms of journal club withdrawal or just need to hear comforting sound of 'epigenetic' now and then, you might have a look at the following recent publications:

**Heroine and DNA methylation:**

Kozlenkov A, et al. [DNA Methylation Profiling of Human Prefrontal Cortex Neurons in Heroin Users Shows Significant Difference between Genomic Contexts of Hyper- and Hypomethylation and a Younger Epigenetic Age.](https://www.ncbi.nlm.nih.gov/pubmed/28556790) Genes (Basel). 2017 May 30;8(6).

**Maternal DNA methyation and offspring bone mass:**

Curtis EM, et al. [Perinatal DNA Methylation at CDKN2A Is Associated With Offspring Bone Mass: Findings From the Southampton Women's Survey.](https://www.ncbi.nlm.nih.gov/pubmed/28419547) J Bone Miner Res. 2017.

**Differentiation potency derived from single-cell transcriptomes:**

Teschendorff AE, Enver T. [Single-cell entropy for accurate estimation of differentiation potency from a cell's transcriptome.](https://www.ncbi.nlm.nih.gov/pubmed/28569836) Nat Commun. 2017 Jun 1;8:15599

**Cool stuff you can do in synthetic biology with DNA methylation:**

Maier JAH, Möhrle R, Jeltsch A. [Design of synthetic epigenetic circuits featuring memory effects and reversible switching based on DNA methylation.](https://www.ncbi.nlm.nih.gov/pubmed/28537256) Nat Commun. 2017 May 24;8:15336.

# May 30, 2017

**Presenter:** Esther Walton

Some of the following may or may not be true:

|  |  |
| --- | --- |
| Inline images 4  ([source](https://en.wikipedia.org/wiki/Physiognomy)) | 1. Dogs tend to look like their owners ([BBC](http://www.bbc.com/future/story/20151111-why-do-dogs-look-like-their-owners)).  2. The government can read your thoughts by EEG ([Brainwave Science LLC](http://www.brainwavescience.com/), see [FAQ](http://www.brainwavescience.com/brainfingerprinting-faqs.html) discussing accuracy; [Michael Flynn](https://www.bloomberg.com/news/articles/2016-12-23/trump-aide-partnered-with-firm-run-by-man-with-alleged-kgb-ties) -- yes that Michael Flynn).  3. A perfectly perpendicular forehead from hair to eyebrows identifies a person with low intelligence ([a Swiss pastor](https://en.wikipedia.org/wiki/Phrenology)).  4. People with deep lines on their foreheads have suffered deeply ([Leonardo da Vinci](https://books.google.co.uk/books?id=oWbkVDljh48C&dq=Leonardo+on+Art+and+the+Artist&q=physiognomy&redir_esc=y#v=onepage&q=%22forehead%20are%20deeply%20marked%22&f=false)).  5. Children whose mothers suffered moderately high depression tend to become aggressive adults. However, a lower amygdala-hippocampal volume ratio is protective ([Journal of Child Psychology and Psychiatry](https://www.ncbi.nlm.nih.gov/pubmed/25424551)). |

Fortunately the following statement has quite a high likelihood of being true:

Tomorrow morning (10:30am in BG7), Esther Walton will tell us about how well amygdala:hippocampus volume ratio can be predicted from DNA methylation:

Walton E, Cecil CAM, Suderman M, Liu J, Turner JA, Calhoun V, Ehrlich S, Relton CL, Barker ED. [Longitudinal epigenetic predictors of amygdala:hippocampus volume ratio](https://www.ncbi.nlm.nih.gov/pubmed/28480579). J Child Psychol Psychiatry. 2017 May 8.

# May 23, 2017

**Presenter:** Matthew Suderman

This week we'll be discussing stem cells:



And then there is [this from the Daily Mash](http://www.thedailymash.co.uk/news/science-technology/is-it-time-to-use-stem-cells-for-practical-jokes-200811201410): "The medical profession faces a new ethical dilemma after scientists raised the prospect of stem cells being used for tomfoolery and high-jinks [...](http://www.thedailymash.co.uk/news/science-technology/is-it-time-to-use-stem-cells-for-practical-jokes-200811201410)"

In particular, tomorrow morning (10:30am in BG7) we'll be discussing how and why induced pluripotent stem cells (iPSCs) differ from regular embryonic stem cells.

Athanasia D. Panopoulos, et al.

[Aberrant DNA Methylation in Human iPSCs Associates with MYC-Binding Motifs in a Clone-Specific Manner Independent of Genetics](https://www.ncbi.nlm.nih.gov/m/pubmed/28388429)

Cell Stem Cell 20, 505–517, April 6, 2017

Other news from epigenetics:

* Esther Walton has another paper, it shows that [amygdala:hippocampal volume ratio](https://www.ncbi.nlm.nih.gov/pubmed/28480579) is associated with DNA methylation in peripheral blood.
* Pathway analysis of smoking associated DNA methylation supports a [role for DNA methylation in smoking-related cancer](https://www.ncbi.nlm.nih.gov/pubmed/28500316).
* [Myocardial infarction is associated with two CpG sites](https://www.ncbi.nlm.nih.gov/pubmed/28515798) near genes previously linked to cardiovascular disease.
* [Weight loss](https://www.ncbi.nlm.nih.gov/pubmed/28517981) is associated small but reproducible changes in DNA methylation.
* DNA Methyltransferase1 (DNMT1) Isoform3 methylates the [mitochondrial genome](https://www.ncbi.nlm.nih.gov/pubmed/28484249). Can you believe we used to think it was Isoform 1?!
* DNA methylation at [midlife is associated with prenatal smoking exposure.](https://www.ncbi.nlm.nih.gov/pubmed/28494218)
* [Temperature-dependent sex determination](https://www.ncbi.nlm.nih.gov/pubmed/28498935) in cucumber appears to be mediated by changes in DNA methylation.

([slides](https://drive.google.com/open?id=1X3781Em7zDd70grD3GhPaoRBAmZgjQ5uR9PtLBlBgtc))

# May 16, 2017

**Presenter:** Charleen Adams

Seems DNA methylation methods development has encountered a bit of a mid-life crisis. After spending much of its life finding ways to estimate and adjust for cell count heterogeneity, it appears to be wondering if all that work was worthwhile. Question is, how will it respond to this crisis:

publish a review denying that it is having a crisis?



publish a position paper proposing completely new directions for methods development?



argue in a letter to the editor in Nature that, "anyways p-value adjustment for multiple testing in GWAS was totally unnecessary"



Tomorrow morning (10:30am BG7), Charleen Adams will present the paper that has triggered the crisis and discuss the most likely response.

Heiss JA, Brenner H. [Impact of confounding by leukocyte composition on associations of leukocyte DNA methylation with common risk factors](https://www.ncbi.nlm.nih.gov/pubmed/28470095). Epigenomics. 2017 May 4.

([slides](https://drive.google.com/open?id=0B-peG00QorQjcW1jcm5scEtnQjZ4NjExV2F2Wm5aTWotQko4))

# May 9, 2017

**Presenter:** Matthew Suderman

Transcription factors (TFs) can be clingy little devils, constantly wanting to put their manky binding domains all over your DNA. Previously we thought we had a solution: methylate and keep on methylating.

Well, it turns out that it's not so simple. According to an international team of scientists, some TFs are so devious as to actually prefer methylated DNA. Gross.

Tomorrow morning (BG7 at 10:30am), I will present this ground-breaking work and discuss how it improves our ability to interpret EWAS findings. A warning though: some individuals may find the images disturbing, some viewers actually decided on the spot to pursue a TF-free lifestyle.

Yin Y, Morgunova E, Jolma A, Kaasinen E, Sahu B, Khund-Sayeed S, Das PK, Kivioja T, Dave K, Zhong F, Nitta KR, Taipale M, Popov A, Ginno PA, Domcke S, Yan J, Schübeler D, Vinson C, Taipale J. [Impact of cytosine methylation on DNA binding specificities of human transcription factors](https://www.ncbi.nlm.nih.gov/pubmed/28473536). Science. 2017 May 5;356(6337)

* Longitudinal predictor of [amygdala:hippocampus volume ratio](https://www.ncbi.nlm.nih.gov/pubmed/28480579)
* [**B cell** EWAS of rheumatoid arthritis](https://www.ncbi.nlm.nih.gov/pubmed/28475762) identifies 64 differentially methylated loci. (*May be interest to asthma EWAS)*
* A small set of genes with [hypomethylated bodies](https://www.ncbi.nlm.nih.gov/pubmed/28115635) tend to be highly expressed and are prone to cancer-associated disregulation.
* Confounding by [blood cell type heterogeneity is a minor issue](https://www.ncbi.nlm.nih.gov/pubmed/28470095) for EWAS of sex, race, age, smoking, alcohol consumption, BMI, cardiovascular fitness, hypertension, coronary heart disease and diabetes.
* Susceptibility to [social defeat stress can be modified by epigenetic editing](https://www.ncbi.nlm.nih.gov/pubmed/28462942) of the Fosb gene.

([slides](https://drive.google.com/open?id=1Aj1Ld5bpFZTI4D_O_RbLxfr2wWCDOfL6q_IvONPtgqI))

# May 2, 2017

**Presenter**: Srikant Ambatipudi

As you know, naughty English words tend to be written with [4 letters](https://en.wikipedia.org/wiki/Four-letter_word) (in Russian, look out for the 3-letter word). There are at least [35](http://www.noswearing.com/fourletterwords.php) (and [counting](http://www.noswearing.com/addslang.php)).

The most worrying acronyms tend to be composed of 3 letters, e.g. BMI, LDL, WHR, ALB, BMD, BMR, CAC, CRP, CVD, FEV, FSG, SBP/DBP, ... and NLR.

Have you measured your neutrophil-to-lymphocyte ratio (NLR) recently? [Apparently](https://www.ncbi.nlm.nih.gov/pubmed/28057051) it should be between 0.78 and 3.53. Values outside this range have been linked to "cardiovascular diseases, infections, inflammatory diseases and in several types of cancers."

Tomorrow morning (BG7 at 10:30am), Srikant Ambatipudi will describe a method for estimating NLR using DNA methylation and its associations with cancer risk and outcomes:

Koestler DC, Usset J, Christensen BC, Marsit CJ, Karagas MR, Kelsey KT, Wiencke JK.

[DNA Methylation-Derived Neutrophil-to-Lymphocyte Ratio: An Epigenetic Tool to Explore Cancer Inflammation and Outcomes.](https://www.ncbi.nlm.nih.gov/pubmed/27965295) Cancer Epidemiol Biomarkers Prev. 2017 Mar;26(3):328-338.

# April 25, 2017

**Presenter**: Doretta Caramaschi ([d.Caramaschi@bristol.ac.uk](mailto:d.Caramaschi@bristol.ac.uk))

Here's a little test. Read the following terms:

* pregnancy
* smoking
* DNA methylation

What pops into your mind?

Was it gene names like AHRR or MYO1G? Okay, you really need to be at tomorrow's journal club. Those genes are so last year. So embarrassing.

Practice these gene names until they roll effortlessly off your tongue: LEKR1, LINC00086, WBP1L and TRIO. And don't go spelling L-I-N-C-0-0-0-8-6 like some dweeb. For those in the know, it's pronounced "/lɪŋk/ 86". And you'll command immediate respect at the next conference if you can calmly drop "cg 2634 on chromosome 3" now and then (referring of course to CpG site "cg27402634").

Tomorrow morning (BG7 at 10:30am), Doretta Caramaschi will tell us everything we need to know about those genes, especially how they may provide a link between prenatal smoking and birthweight.

Morales E, Vilahur N, Salas LA, Motta V, Fernandez MF, Murcia M, Llop S, Tardon A, Fernandez-Tardon G, Santa-Marina L, Gallastegui M, Bollati V, Estivill X, Olea N, Sunyer J, Bustamante M. [Genome-wide DNA methylation study in human placenta identifies novel loci associated with maternal smoking during pregnancy.](https://www.ncbi.nlm.nih.gov/pubmed/27591263) Int J Epidemiol. 2016 Oct;45(5):1644-1655. Epub 2016 Sep 1. PMID: 27591263

# April 11, 2017

**Presenter:** Matthew Suderman

Tomorrow morning (10:30am, BG7) we will be discussing the biology of two different diets: calorie restriction and an immensely popular diet among ancient aristocrats called 'ad libitum'.

Proponents of calorie restriction claim that it increases longevity while 'ad libitum' proponents have protested that the effects of calorie restriction are merely subjective, that time only *seems* to pass slower with fewer calories.

But now a mouse study threatens to make the debate more objective: 'ad libitum' dieters have longer chain fatty acids in their livers, making them, as they say, 'longer livers'. Quod erat demonstrandum.

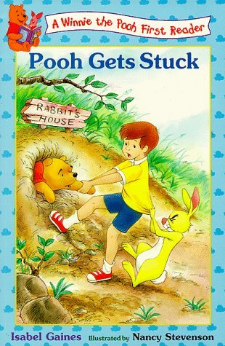
Hahn O, Grönke S, Stubbs TM, Ficz G, Hendrich O, Krueger F, Andrews S, Zhang Q, Wakelam MJ, Beyer A, Reik W, Partridge L. [Dietary restriction protects from age-associated DNA methylation and induces epigenetic reprogramming of lipid metabolism](https://www.ncbi.nlm.nih.gov/pubmed/28351387). Genome Biol. 2017 Mar 28;18(1):56.

([slides](https://drive.google.com/open?id=16F1D8KcNyOYQE_7y4N0ljqUQK93OfMbiiWSWtMxTPyo))

# April 4, 2017

**Presenter:** Matthew Suderman

Your response to the following book cover is likely dependent on your current grasp of English, knowledge of modern English literature, current mood and most important maturity level.



([Why not buy a copy on amazon?](https://www.amazon.com/Pooh-Gets-Stuck/dp/0786843616/ref=sr_1_1?s=books&ie=UTF8&qid=1491222604&sr=1-1&keywords=pooh+gets+stuck))

The response of the genome to DNA methylation is analogous. While you've likely heard that DNA methylation near the beginning of a gene is repressive, you might not have heard that DNA methylation *within the body of a gene* is positively associated with gene activity.

Tomorrow morning (10:30am in BG7), we will discuss a possible reason for this positive correlation:

Neri F, Rapelli S, Krepelova A, Incarnato D, Parlato C, Basile G, Maldotti M, Anselmi F, Oliviero S. [Intragenic DNA methylation prevents spurious transcription initiation.](https://www.ncbi.nlm.nih.gov/pubmed/28225755)  
Nature. 2017 Mar 2;543(7643):72-77. doi: 10.1038/nature21373. Epub 2017 Feb 22.  
PMID: 28225755

([slides](https://drive.google.com/open?id=1VF8edvBqxK5aJpWVSQRk_7peKPXsqwnI_nD_WU4V3_A))

# March 28, 2017

**Presenter:** Rebecca Richmond

*Rebecca Richmond went to work on smoking mediation,*

*Heeded warning and used Mendelian Randomization.*

*Bestowed insight by network ny poetics,*

*Compared to folate and now in Epigenomics.*

Tomorrow morning (BG7, 10:30am), Rebecca Richmond herself, now immortalised in poetry, will fill us in on the full story:

Richmond RC, Joubert BR.

[Contrasting the effects of intra-uterine smoking and one-carbon micronutrient exposures on offspring DNA methylation.](https://www.ncbi.nlm.nih.gov/pubmed/28234021)

Epigenomics. 2017 Mar;9(3):351-367. doi: 10.2217/epi-2016-0135. Epub 2017 Feb 17.

PMID: 28234021

# March 21, 2017

**Presenter:** Matthew Suderman

Are you worried about being one of the millions who die prematurely every year due from air pollution? Well you can stop worrying now by regularly taking our patented ClearTheAir™ tablets. They were designed based on cutting edge epigenetic research to fully reverse the effects of air pollution. One of our satisfied customers is even avoiding lung cancer by taking one tablet with every cigarette. We invite you to breath easier with ClearTheAir™.

**Disclaimer:**

Please note that the information provided here is for personal information only and should not replace medical advice from a qualified practitioner. The (Epi)genetics Journal Club accepts no responsibility for how you choose to act on this information. The journal club does however accept many other things, like money for example.

Zhong J, Karlsson O, Wang G, Li J, Guo Y, Lin X, Zemplenyi M, Sanchez-Guerra M, Trevisi L, Urch B, Speck M, Liang L, Coull BA, Koutrakis P, Silverman F, Gold DR, Wu T, Baccarelli AA.  
[B vitamins attenuate the epigenetic effects of ambient fine particles in a pilot human intervention trial.](https://www.ncbi.nlm.nih.gov/pubmed/28289216) Proc Natl Acad Sci U S A. 2017 Mar 13. pii: 201618545.

([slides](https://drive.google.com/open?id=15YGU-LnFkBItgkyj5rpBW2pbYcasK91qmW1kPfyfgeQ))

# March 14, 2017

**Presenter:** Paul Yousefi

What do methylSpectrum, RefFreeEWAS, EWASher, CellCDec, Refactor, CIBERSORT, and MethylPurify have in common?

(a) Party drugs of choice for epigeneticists.

(b) Gift soap brands for the epigeneticist who has everything.

(c) The collective works of the band Convulsive Epigenetica.

(d) Chapter titles of an unpublished novel written by a disillusioned epigeneticist.

(e) Names of software tools for addressing cell count hetergeneity in DNA methylation.

Tomorrow morning (BG7, 10:30am), Paul Yousefi will provide the correct answer to this question and then present the latest of these: EpiDISH ... hold, on ... breaking news ... another one just appeared on [bioarxiv](http://biorxiv.org/content/early/2017/02/28/112417). Sorry Paul but your presentation tomorrow is already out of date.

Teschendorff AE, Breeze CE, Zheng SC, Beck S. [A comparison of reference-based algorithms for correcting cell-type heterogeneity in Epigenome-Wide Association Studies](https://www.ncbi.nlm.nih.gov/pubmed/28193155). BMC Bioinformatics. 2017 Feb 13;18(1):105.

# March 7, 2017

**Presenter:** Gemma Sharp

*"Of particular concern is the U.S. Black population, who continues to suffer from the highest prevalence of PTB [preterm birth] (∼17%) in the world."*

Tomorrow morning, Gemma Sharp will describe possible associations of PTB with DNA methylation in maternal blood and a surprising lack of associations in cord blood (10;30am in BG7):

Hong X, et al. [Genome-wide DNA Methylation Associations with Spontaneous Preterm Birth in US Blacks: Findings in Maternal and Cord Blood Samples.](https://www.ncbi.nlm.nih.gov/m/pubmed/28165855/?i=1&from=/28165855/related) Epigenetics. 2017.

# February 28, 2017

**Presenter:** Matthew Suderman

Tomorrow morning (BG7, 10:30am) we bring you a tale of two gestational age calculators. They were published at the same time and in the same journal, and yet they are not brethren. It will be for you to discern between the wise and the foolish, but beware for even Satan himself has been known to masquerade as an angel of light.

Knight AK, Craig JM, Theda C, Bækvad-Hansen M, Bybjerg-Grauholm J, Hansen CS, Hollegaard MV, Hougaard DM, Mortensen PB, Weinsheimer SM, Werge TM, Brennan PA, Cubells JF, Newport DJ, Stowe ZN, Cheong JL, Dalach P, Doyle LW, Loke YJ, Baccarelli AA, Just AC, Wright RO, Téllez-Rojo MM, Svensson K, Trevisi L, Kennedy EM, Binder EB, Iurato S, Czamara D, Räikkönen K, Lahti JM, Pesonen AK, Kajantie E, Villa PM, Laivuori H, Hämäläinen E, Park HJ, Bailey LB, Parets SE, Kilaru V, Menon R, Horvath S, Bush NR, LeWinn KZ, Tylavsky FA, Conneely KN, Smith AK. [An epigenetic clock for gestational age at birth based on blood methylation data.](https://www.ncbi.nlm.nih.gov/pubmed/27717399) Genome Biol. 2016 Oct 7;17(1):206.

Bohlin J, Håberg SE, Magnus P, Reese SE, Gjessing HK, Magnus MC, Parr CL, Page CM, London SJ, Nystad W. [Prediction of gestational age based on genome-wide differentially methylated regions.](https://www.ncbi.nlm.nih.gov/pubmed/27717397) Genome Biol. 2016 Oct 7;17(1):207.

([slides](https://drive.google.com/open?id=1pD3KtI7weqB671w3wKO7gik6kKffCYfnhDlW1ctdCOo))

# February 21, 2017

**Presenter**: Rebecca Richmond ([Rebecca.Richmond@bristol.ac.uk](mailto:Rebecca.Richmond@bristol.ac.uk))

In January, two large epigenome-wide association studies of BMI were published. We had a look at the [first study (Wahl et al)](https://www.ncbi.nlm.nih.gov/pubmed/28002404) a couple of weeks ago. I've peaked at the [second study (Mendelson et al](https://www.ncbi.nlm.nih.gov/pubmed/28095459)) and now I'm in turmoil: each study identifies *different* single CpG sites whose methylation levels appear to influence BMI. The evidence for Mendelson's site inside the SREBF1 gene appears strong, but how can it not be Wahl's site near N*FAT*C2IP?!

Tomorrow morning (10:30am, BG7), Rebecca Richmond will present the Mendelson study and help us evaluate the evidence.

Mendelson, et al. [Association of Body Mass Index with DNA Methylation and Gene Expression in Blood Cells and Relations to Cardiometabolic Disease: A Mendelian Randomization Approach](https://www.ncbi.nlm.nih.gov/pubmed/28095459). PLoS Med. 2017 Jan 17;14(1):e1002215.

Other news:

* [EpiDISH appears to be better at estimating cell counts](https://www.ncbi.nlm.nih.gov/pubmed/28193155) than the Houseman algorithm.
* We didn't see strong evidence for this ALSPAC but ... in another larger study [epigenetic age appeared to be accelerated by certain lifestyle factors](https://www.ncbi.nlm.nih.gov/pubmed/28198702).
* Protein expression = gene expression? Not always! [Paternal deprivation in prairie voles](https://www.ncbi.nlm.nih.gov/pubmed/27998780) decreases CRHR2 gene expression while increasing CRHR2 protein expression in males.
* When we start analysing whole genome bisulfite sequencing datasets, we should consider using [ABBA to identify differentially methylated regions](https://www.ncbi.nlm.nih.gov/pubmed/28213474).
* [EWAS of obesity in adipose tissue and peripheral blood](https://www.ncbi.nlm.nih.gov/pubmed/28211912) was used to identify CpG sites correlated between the tissues and associated with obesity.
* [Coffee consumption](https://www.ncbi.nlm.nih.gov/pubmed/28198392) may be associated with DNA methylation in blood.
* REPTILE is better than previous methods at [identifying enhancer regions](https://www.ncbi.nlm.nih.gov/pubmed/28193886).

([slides](https://drive.google.com/open?id=0B-peG00QorQjMm5RZzFhcklmaXRRLW5KdFp5Yng1UkRySTMw))

# February 14, 2017

**Presenter**: Anna Guyatt

Tomorrow morning (10:30am in BG7), our very own cupid whisperer, Anna Guyatt, will present the latest approach to painless match-making both in life and in GWAS. If you've ever wanted to play cupid or have tried and failed, this presentation could change your life. It is rumoured that a demonstration may take place, but no word yet if the arrow tip be gold or lead.

Liu JZ, Erlich Y, Pickrell JK.

[Case-control association mapping by proxy using family history of disease.](https://www.ncbi.nlm.nih.gov/pubmed/28092683)

Nat Genet. 2017 Jan 16. doi: 10.1038/ng.3766.

([slides](https://drive.google.com/open?id=0B-peG00QorQjN2FSa1lWcW1EVmc) -- do have a look, lots of a bonus content!)

In other news:

* The relationship between [**DNA methylation and gene expression**](https://www.ncbi.nlm.nih.gov/pubmed/28168293) is complicated, but perhaps the ME-Class model can help.
* EWAS methods are changing. A new method tests [**mean and variance differences while taking into account correlations between CpG sites**](https://www.ncbi.nlm.nih.gov/pubmed/28165116).
* The maternal methylome appears to be more relevant to [**preterm birth**](https://www.ncbi.nlm.nih.gov/pubmed/28165855) than the cord methylome.
* [**Paternal low fat diet**](http://www.sciencedirect.com/science/article/pii/S0925443917300509) appears to increase skeletal size but with reduced bone density.

# February 7, 2017

**Presenter**: Srikant Ambatipudi

Tomorrow morning, Srikant Ambatipudi will follow in the footsteps of Adolphe Quetelet with a poetic rendition of the following publication (10:30am in BG7):

Wahl, et al. [Epigenome-wide association study of body mass index, and the adverse outcomes of adiposity](https://www.ncbi.nlm.nih.gov/pubmed/28002404). Nature. 2017 Jan 5;541(7635):81-86. doi: 10.1038/nature20784.

PMID: 28002404

So who was Adolphe Quetelet?

1. In 1832, he was the first to propose BMI as an index of obesity, about 130 years before it became popular to study.
2. To many he is considered a founder of the social sciences for his use of statistics to understand society.
3. When he wrote, flower gardens bloomed:
4. *e.g.* "we are struck with the inflexible constancy of the laws which regulate the march of worlds, and which preside over the succession of human generations."
5. *e.g.* "The Supreme has then not only spread life and movement throughout, and willed that its impress should be preserved, but has done more; for he has permitted man to associate in some degree with his work, and to modify it."

Seems he's suggesting that BMI is mostly predetermined but that cake club can have an effect.

In other news:

* Inorganic **arsenic** appears to do some of it's dirty work by [inhibiting CTCF](https://www.ncbi.nlm.nih.gov/pubmed/28150704) binding of DNMTs resulting in genome-wide DNA methylation changes.
* Just like [global DNA demethylation](https://www.ncbi.nlm.nih.gov/pubmed/28147265) is a normal part of cell reprogramming, it also occurs during the derivation of **induced pluripotent stem cells**. Could this have implications for the use of iPSC to investigate pre-iPSC exposures?
* In utero exposure to **maternal smoking** reduces neuronal content in the [fetal dorsolateral prefrontal cortex](https://www.ncbi.nlm.nih.gov/pubmed/28149327).
* **Single-cell** chromatin state profiles show that K562 leukemic cells are quite [heterogeneous](https://www.ncbi.nlm.nih.gov/pubmed/28118844).

# January 31, 2017

**Presenter**: Matthew Suderman

Tomorrow morning (10:30am, BG7), I will present yet another paper about epigenetics and cigarette smoking. What's new about this paper is their use of whole-genome bisulfite sequencing rather than Illumina microarrays. Their results suggest that much of the genome most relevant to environmental exposure are not covered by the microarray.

Bauer, et al.

[Environment-induced epigenetic reprogramming in genomic regulatory elements in smoking mothers and their children.](https://www.ncbi.nlm.nih.gov/pubmed/27013061)

Mol Syst Biol. 2016 Mar 24;12(3):861. doi: 10.15252/msb.20156520.

Thought you might be amazed by some remarkably prescient ads from the past:



(How did Lucky's know that smoking would have a stronger affect on DNA methylation than BMI?​ Amazing.)

([slides](https://docs.google.com/a/bristol.ac.uk/presentation/d/1VOt5mO_g9qZhQHChaFJKs7e-KAsibZgFCI7PC0LyqJk/edit?usp=sharing))

* [Genetic Variants in Epigenetic Pathways and Risks of Multiple Cancers in the GAME-ON Consortium. In a meta-analysis of 50K cases and 50K controls,](http://www.ncbi.nlm.nih.gov/pubmed/28115406) 8 of 555 genes involved in epigenetic processes contained genetic variants associated with risk of more than cancer type.
* [Pluripotent cells display enhanced resistance to mutagenesis.](http://www.ncbi.nlm.nih.gov/pubmed/28129601)
* [A molecular roadmap for induced multi-lineage trans-differentiation of fibroblasts by chemical combinations.](http://www.ncbi.nlm.nih.gov/pubmed/28128194) "we find that mouse embryonic fibroblast cells can be induced to trans-differentiate into a wide range of somatic lineages simultaneously by treatment with a combination of four chemicals”. They investigate the results in detail using various genomic analyses including single cell analysis.
* [Stability of the human sperm DNA methylome to folic acid fortification and short-term supplementation](https://www.ncbi.nlm.nih.gov/pubmed/27994001). "short-term exposure to low-dose folic acid supplements of 400 μg/day, over a period of 3 months … has no major impact on the sperm DNA methylome”.
* [Epigenetic profiling of ADHD symptoms trajectories: a prospective, methylome-wide study.](https://www.ncbi.nlm.nih.gov/pubmed/27217153) A paper by our very own Esther Walton! "We found that DNA methylation at birth differentiated ADHD trajectories across multiple genomic locations ... None of these probes maintained an association with ADHD trajectories at age 7.”
* [Traffic-derived particulate matter exposure and histone H3 modification: A repeated measures study](https://www.ncbi.nlm.nih.gov/pubmed/27918982). "Our results suggest a possible role of global histone H3 modifications in effects of traffic-derived PM exposures”

# January 24, 2017

**Presenter**: Esther Walton

I'm so sorry to have to deliver this disappointing news: the Children of the 90s, children we know better than even our own, have been using addictive substances for several years. They are arguing that their methylome made them do it. Tomorrow morning at 10:30am (in **BG7**), Esther Walton will lay out the evidence and allow you to decide.

Cecil CA, Walton E, Smith RG, Viding E, McCrory EJ, Relton CL, Suderman M, Pingault JB, McArdle W, Gaunt TR, Mill J, Barker ED. [DNA methylation and substance-use risk: a prospective, genome-wide study spanning gestation to adolescence](https://www.ncbi.nlm.nih.gov/pubmed/27922636). Transl Psychiatry. 2016 Dec 6;6(12):e976. doi: 10.1038/tp.2016.247.

In other news:

* DNA methylation may account for 6% of the variation of **C-reactive protein** beyond sex, age and genetic differences according to a large [meta-analysis](https://www.ncbi.nlm.nih.gov/pubmed/27955697).
* DNA methylation appears to mediate the effects of some **psychiatric trait** associated genetic variants on gene expression [in adolescents](http://www.nature.com/tp/journal/v7/n1/full/tp2016275a.html).
* Safe levels of **Bisphenol A** are probably a lot lower than we thought according to a [rat study](http://www.nature.com/articles/srep40337).
* [13%](https://www.ncbi.nlm.nih.gov/pubmed/28067913) of HPV-negative **head and neck** squamous cell carcinomas appear to have developed due to impaired H3K36 methylation.
* **BMI** is associated with methylation at 187 CpG sites according to a large [meta-analysis](https://www.ncbi.nlm.nih.gov/pubmed/28002404).
* Over [14,000 CpG sites](https://bmcgenomics.biomedcentral.com/articles/10.1186/s12864-016-3452-1) have continuously changing methylation levels from **age 0 to 8**.
* A new R package [SMITE](https://bmcbioinformatics.biomedcentral.com/articles/10.1186/s12859-017-1477-3) creates network modules by **integrating genomic and epigenomic data**.

# January 17, 2017

**Presenter:** Kim Burrows ([Kimberley.Burrows@bristol.ac.uk](mailto:Kimberley.Burrows@bristol.ac.uk))

The suspense is [so painful](http://www.tubechop.com/watch/8792693) . It's been a month since we heard Part 1 of [Bonder et al. (Nat Genet. 2016)](https://www.ncbi.nlm.nih.gov/pubmed/27918535), but now the wait is nearly over. Kim Burrows will present Part 2 tomorrow at 10:30am in **OS6**, that's right OS6.

Here is a short summary (spoiler alert!):

We're pretty comfortable with how genetic variants might affect methylation levels at nearby (cis) CpG sites. Distant (trans) effects are a bit more mysterious. The authors show that genetic variants linked to diseases are responsible for many of the trans effects. They show that these effects are achieved in three steps:

1. the genetic variants influence the expression of nearby transcription factors (including your favourites: NFKB1, CTCF and NKX2-3).

2. the expression differences result in more or less transcription factor binding throughout the genome.3. where binding is different, methylation is correspondingly different.

Bonder, et al. [Disease variants alter transcription factor levels and methylation of their binding sites](https://www.ncbi.nlm.nih.gov/pubmed/27918535). Nat Genet. 2016 Dec 5.

Over the centuries the Dutch have made many important contributions to the world. A [recent survey](http://www.eupedia.com/forum/threads/16865-Greatest-Dutch-contributions-to-the-world) identified the most important: liberal laws, paintings, microscope, telescope, pendulum clock, mercury thermometer, electronic media, New York, Heineken and Gouda cheese. A more recent but no less important contribution has been several researchers to the IEU. In fact, if any more Dutch is spoken, [zoute drop](https://www.youtube.com/watch?v=jb2UWhtvNA8) trafficked or [opinions](http://www.hollandsbest.com/pins_magnets/images/pin_12725_opinionated.jpg) shared in office BS10, it may be declared extraterritorial ([it's happened before](https://en.wikipedia.org/wiki/Princess_Margriet_of_the_Netherlands)).

# December 20, 2017

Tomorrow morning at 10:30 in BG7, Kim Burrows will tell a tale of yet another considerable contribution: blood donations by 3,841 Dutch individuals to generate genetic, methylation and gene expression profiles.

Bonder, et al. [Disease variants alter transcription factor levels and methylation of their binding sites](https://www.ncbi.nlm.nih.gov/pubmed/27918535). Nat Genet. 2016 Dec 5.

# December 13, 2016

**Presenter**: Matthew Suderman ([matthew.suderman@bristol.ac.uk](mailto:matthew.suderman@bristol.ac.uk))

For most cancers, being male increases risk. The current leading hypothesis was best stated by Mark Twain: "Man was made at the end of the week’s work, when God was tired [and forgot the extra X chromosome]". Tomorrow morning at 10:30am in BG7 we will discuss the implications for cancer risk:

Dunford A, Weinstock DM, Savova V, Schumacher SE, Cleary JP, Yoda A, Sullivan TJ, Hess JM, Gimelbrant AA, Beroukhim R, Lawrence MS, Getz G, Lane AA.

[Tumor-suppressor genes that escape from X-inactivation contribute to cancer sex bias.](https://www.ncbi.nlm.nih.gov/pubmed/27869828)

Nat Genet. 2016 Nov 21.

([slides](https://drive.google.com/open?id=1TuL5gPj6y6Nnw0O7RyOQlZmVvPYj5A8cKi-29_eT0JU))

# December 6, 2016

**Presenter**: Matthew Suderman ([matthew.suderman@bristol.ac.uk](mailto:matthew.suderman@bristol.ac.uk))

We were the first to look at associations with birthweight in longitudinal measurements of DNA methylation ([Simpkin et al. 2015](https://www.ncbi.nlm.nih.gov/pubmed/25869828)). We found that associations identified at birth had resolved by early childhood, but now a recent publication reports that some associations may still be present in mid-childhood:

[Birth weight-for-gestational age is associated with **DNA** **methylation** at birth and in childhood.](https://www.ncbi.nlm.nih.gov/pubmed/27891191)

Agha G, Hajj H, Rifas-Shiman SL, Just AC, Hivert MF, Burris HH, Lin X, Litonjua AA, Oken E, DeMeo DL, Gillman MW, Baccarelli AA.

Clin Epigenetics. 2016 Nov 16;8:118.

PMID: 27891191

Tomorrow morning at 10:30am in BG7 we will investigate this apparent contradiction. We'll consider all relevant factors including a possible link to the length of Andrew's hair at the time of our analyses. Although the length function has many discontinuities, we do have plenty of data points and will make generous use of a smoothing function.



([slides](https://docs.google.com/a/bristol.ac.uk/presentation/d/1gnnxW9yi9Jj6bzZ57SCsDyJyE0VkDw6WSNVn0c3qqpU/edit?usp=sharing))

# November 29, 2016

**Presenter**: Lotte Houtepen ([lotte.houtepen@bristol.ac.uk](mailto:lotte.houtepen@bristol.ac.uk))

First with smoking and now with alcohol, epigenetics is finding ways to uncover your favourite vices. What will it be next? Will it be something legal or illegal?

Tomorrow morning at 10:30am in BG7, Lotte Houtepen will present a surprisingly good biomarker for alcohol intake:

Liu, et al. [A DNA methylation biomarker of alcohol consumption](https://www.ncbi.nlm.nih.gov/pubmed/27843151). Mol Psychiatry. 2016 Nov 15. doi: 10.1038/mp.2016.192.

# November 22, 2016

**Presenter**: Anna Guyatt ([anna.guyatt@bristol.ac.uk](mailto:anna.guyatt@bristol.ac.uk))

Tomorrow at 10am in BG10, Anna Guyatt will present evidence that:

"common SNPs explain 21% of the variation in social deprivation and 11% of household income."

Hill WD, Hagenaars SP, Marioni RE, Harris SE, Liewald DC, Davies G, Okbay A, McIntosh AM, Gale CR, Deary IJ. [Molecular Genetic Contributions to Social Deprivation and Household Income in UK Biobank.](https://www.ncbi.nlm.nih.gov/pubmed/27818178) Curr Biol. 2016 Oct 31. pii: S0960-9822(16)31119-8. doi: 10.1016/j.cub.2016.09.035.

If you find that depressing, then you really need to join our journal club where we've found that simply inserting 'epi' in front of a word makes it more hopeful. Here are some examples:

1. critic: What is more negative that a critic? Epicritics are nerves in the skin that are capable of fine discrimination of touch.

2. demiology: Demiology is not even a word, but add epi- and you have one of the most noble of academic disciplines.

3. blast: A blast is a destructive wave of compressed air, but an epiblast is part of a developing embryo, the beginning of a new life.

4. phenomenon: A phenomenon is a fact or situation that is observed to exist or happen. With an epiphenomenon we have a secondary effect or byproduct, a welcome distraction if you will from hard realities just like this email is to that grant application you still haven't finished.

# November 15, 2016

**Presenter**: Matthew Suderman ([matthew.suderman@bristol.ac.uk](mailto:matthew.suderman@bristol.ac.uk))

What's so important about genomic imprinting you ask? Well, it's possibly the reason why your oocyte became a fully functioning human rather than getting stuck as an ovarian teratoma. But before you congratulate yourself for being Mother Nature's blessed child, you should also know that she selected much of your imprinting patterns, not with love, but with a deck of cards.

Tomorrow morning at 10:30am in BG7 we'll discuss evidence for transient and stochastic patterns of imprinting:

Sanchez-Delgado M, Court F, Vidal E, Medrano J, Monteagudo-Sánchez A, Martin-Trujillo A, Tayama C, Iglesias-Platas I, Kondova I, Bontrop R, Poo-Llanillo ME, Marques-Bonet T, Nakabayashi K, Simón C, Monk D. [Human Oocyte-Derived Methylation Differences Persist in the Placenta Revealing Widespread Transient Imprinting.](https://www.ncbi.nlm.nih.gov/pubmed/27835649) PLoS Genet. 2016 Nov 11;12(11):e1006427.

([slides](https://drive.google.com/open?id=1t6OYhAM89CQXw55bUagwVMAXEmkY-sO7gRADCIlkbDU))

# November 8, 2016

**Presenter**: Matthew Suderman ([matthew.suderman@bristol.ac.uk](mailto:matthew.suderman@bristol.ac.uk))

Epigenetic mechanisms exist likely because variation improves chances of survival. Epigenome-wide association studies investigate inter-individual variation, epigenetic differences linked to exposure or phenotypes. Epigenetic mechanisms also make Intra-individual variation possible and has not been studied all that much. Tomorrow morning at 10:30am in BG7, we'll look at one way to investigate intra-individual variation using genome-wide data:

Ecker, et al. Genome-wide Analysis of Differential Transcriptional and Epigenetic Variability Across Human Immune Cell Types. [bioRxiv 083246; doi: http://dx.doi.org/10.1101/083246](http://dx.doi.org/10.1101/083246)

([slides](https://drive.google.com/open?id=12CsR2l7RfBy6cF2neEz38v4cGA0mlObxW2ePWmHoy-Q))

# November 1, 2016

Cancelled this week.

No journal club tomorrow as several of us will be attending Epigenomics of Common Diseases 2016. Wish us luck as we attempt to wow the world with our research wares and silently supplicate the gods of science for sage insights.

That said, some interesting epigenetics has been published. The following paper presents evidence that "TET2 expression and 5hmC abundance are significantly altered in the umbilical veins of GDM

and preeclampsia". Keep in mind though that sample size was low and there may be some analysis concerns.

Sun M, Song MM, Wei B, Gao Q, Li L, Yao B, Chen L, Lin L, Dai Q, Zhou X, Tao J, Chen J, He C, Jin P, Xu Z. [5-Hydroxymethylcytosine-mediated alteration of transposon activity associated with the exposure to adverse in utero environments in human.](https://www.ncbi.nlm.nih.gov/pubmed/27005421) Hum Mol Genet. 2016 Jun 1;25(11):2208-2219.

# October 25, 2016

**Presenter**: Matthew Suderman ([matthew.suderman@bristol.ac.uk](mailto:matthew.suderman@bristol.ac.uk))

Would you believe that it is possible to convert fibroblasts to neurons without interrupting epigenetic age estimates? One day these kinds of approaches will allow us to generate all 200 cell types from skin cells collected from ALSPAC participants. We'll then do epidemiology by analyzing the responses of these cells to thousands of different exposures.

In the meantime, we'll have journal club. See you tomorrow, BG10 at 10am:

Huh CJ, Zhang B, Victor MB, Dahiya S, Batista LF, Horvath S, Yoo AS.

[Maintenance of age in human neurons generated by microRNA-based neuronal conversion of fibroblasts.](https://www.ncbi.nlm.nih.gov/pubmed/27644593) Elife. 2016 Sep 20;5. pii: e18648. doi: 10.7554/eLife.18648.

([slides](https://drive.google.com/open?id=1WojjgJUSmaNT8Pijpz4XGvaQ7eoJrMgnckjJyUxxRM8))

# October 18, 2016

**Presenter**: Matthew Suderman ([matthew.suderman@bristol.ac.uk](mailto:matthew.suderman@bristol.ac.uk))

For a good time, see what the internet says about your chances of living to 100:

<http://deathclock.com/>

<https://www.death-clock.org/>

<http://www.findyourfate.com/deathmeter/deathmtr.html>

<http://deathtimer.com/>

<https://www.sunlife.co.uk/life-cover/over-50-life-insurance/death-clock/>

Take your pick, I dare you. Better yet, try them all to get a confidence interval. Responses vary but all promise to remind you that "life is slipping away ... second by second."

I suspect that we epigeneticists could be much more accurate than these websites given a bit of blood and findings from a recent meta-analysis (<https://www.ncbi.nlm.nih.gov/pubmed/27690265>). And it seems that there is still room for improvement: a new epigenetic clock was just published that provides improved estimates of cancer risk. It's called epiToc ... did you hear that? epi-Toc epi-Toc epi-Toc ...

We'll discuss the epiToc tomorrow at 10:30am in BG7:

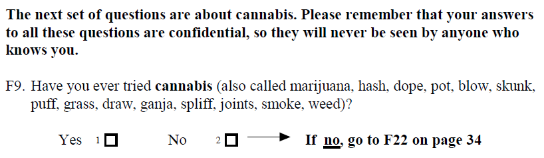
Yang Z, Wong A, Kuh D, Paul DS, Rakyan VK, Leslie RD, Zheng SC, Widschwendter M, Beck S, Teschendorff AE. [Correlation of an epigenetic mitotic clock with cancer risk](https://www.ncbi.nlm.nih.gov/pubmed/27716309). Genome Biol. 2016 Oct 3;17(1):205.

([slides](https://drive.google.com/open?id=1kzTIchCW4_JkTrYufTkqMNVG0upe6XH2yz8dZgwwCPQ))

# October 11, 2016

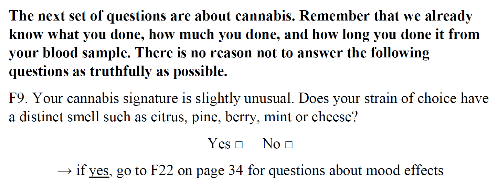
**Presenter**: Leanne Küpers ([leanne.kupers@bristol.ac.uk](mailto:leanne.kupers@bristol.ac.uk))

Cohort study questionnaires today have many obvious limitations, e.g.



Will the participant answer truthfully? Has the question included the term used by the younger generation?

In the future, biological samples will provide some of this information directly allowing questionnaires to become more personal and precise:



Tomorrow morning at 10:30am in BG7, Leanne Küpers will describe a first step in using DNA methylation profiles to uncover exposure histories:

Reese et al.[DNA Methylation Score as a Biomarker in Newborns for Sustained Maternal Smoking during Pregnancy](http://www.ncbi.nlm.nih.gov/pubmed/27323799). Environ Health Perspect. 2016 Jun 21.

# October 4, 2016

**Presenter**: Matthew Suderman ([matthew.suderman@bristol.ac.uk](mailto:matthew.suderman@bristol.ac.uk))

I know, I know, ever since Bakulski et al. ([Epigenetics, 2016](https://www.ncbi.nlm.nih.gov/pubmed/27019159)) published their cord blood DNA methylation reference you've been wondering about the nRBC cell type that they included in the reference. I certainly have. Why didn't all the other cord blood references include nRBCs? How many nRBCs are there in cord blood? Do they tell us something important? Tomorrow morning at 10:30am (in BG7) we'll hopefully settle some of these burning questions with the help of the following recent publication:

de Goede OM, Lavoie PM, Robinson WP. [Characterizing the hypomethylated DNA methylation profile of nucleated red blood cells from cord blood.](https://www.ncbi.nlm.nih.gov/pubmed/27687885) Epigenomics. 2016 Sep 30.

([slides](https://drive.google.com/open?id=1O1UmvlxexS8mT13Uf9ZEhzeYKxe0uk_VDHsO7WFR7ik))

# September 27, 2016

**Presenter**: Matthew Suderman ([matthew.suderman@bristol.ac.uk](mailto:matthew.suderman@bristol.ac.uk))

Might manipulations of living cells become as important a tool to epidemiology as statistical tests?

Tomorrow at 10:30am (in BG7) we will discuss a recent study showing that cells collected from individuals with a history of trauma and addiction respond differently to stress hormones:

Yeo S, Enoch MA, Gorodetsky E, Ahktar L, Schuebel K, Roy A, Goldman D. [The influence of FKBP5 genotype on expression of FKBP5 and other glucocorticoid-regulated genes, dependent on trauma exposure.](http://www.ncbi.nlm.nih.gov/pubmed/27648526) Genes Brain Behav. 2016 Sep 20. doi: 10.1111/gbb.12342.

([slides](https://drive.google.com/open?id=1RD-29YuBLsZWfpYUiSlA-C9tsvqocLq3HSAMoDQgbp8))

# September 20, 2016

**Presenter**: Matthew Suderman ([matthew.suderman@bristol.ac.uk](mailto:matthew.suderman@bristol.ac.uk))

A recent GWAS identified 108 loci associated with schizophrenia, many with the kinds of p-values that academic dreams are made of. And then the alarm clock rudely interrupted with the discovery that only 10 loci could be linked to protein coding differences and only 12 to changes in gene expression.

Tomorrow morning at 10.30h in BG7, we will discuss evidence that many of these loci are linked to changes in DNA methylation:

Hannon, et al. [An integrated genetic-epigenetic analysis of schizophrenia: evidence for co-localization of genetic associations and differential DNA methylation.](http://www.ncbi.nlm.nih.gov/pubmed/27572077) Genome Biol. 2016 Aug 30;17(1):176

([slides](https://docs.google.com/a/bristol.ac.uk/presentation/d/1fG7znv3ySJqlq-QBEerhL097aS2owmrP4LJPwOCx6nQ/edit?usp=sharing))

# September 13, 2016

**Presenter**: Matthew Suderman ([matthew.suderman@bristol.ac.uk](mailto:matthew.suderman@bristol.ac.uk))

Steve Horvath has been at it again, this time describing a method for estimating immune age using DNA methylation. His results he says "provide additional context towards resolving several controversial, epidemiological paradoxes":

1. **Hispanic paradox**: Hispanics in the USA have lower overall risk of mortality despite having a disadvantaged risk profile.

2. **Black-white mortality crossover**: After age 85, African Americans have lower mortality rates despite having higher prior mortality rates.

3. **Tismane inflammation paradox**: The Tsimane have higher levels of inflammation and infection and low HDL levels but without accelerated cardiovascular aging.

4. **Sex morbidity-mortality paradox**: Women have lower age-adjusted mortality than men despite having a greater incident of comorbid conditions.

5. **The 2=1 paradox**: Suppose that a = 1. Then, a\*a = a and a\*a - 1 = a - 1. If we divide by a - 1, then we see that a + 1 = 1. Therefore, 1 + 1 = 1.

See you tomorrow morning at 10.30h in BG7!

Horvath et al. [An epigenetic clock analysis of race/ethnicity, sex, and coronary heart disease](https://www.ncbi.nlm.nih.gov/pubmed/27511193). Genome Biol. 2016 Aug 11;17(1):171. doi: 10.1186/s13059-016-1030-0.

([slides](https://docs.google.com/a/bristol.ac.uk/presentation/d/1fZcmX861nMovHRuUjgg_bfkILRFv7PC75QEcNW2G6sQ/edit?usp=sharing))

# September 6, 2016

**Presenter**: Matthew Suderman ([matthew.suderman@bristol.ac.uk](mailto:matthew.suderman@bristol.ac.uk))

Some have suggested that the NHS save money by denying non-life threatening surgery to anyone with BMI > 30 until they had lost 10% of their body weight.

<https://www.theguardian.com/society/2016/sep/03/vale-of-york-nhs-obesity-smokers-deny-elective-surgery>

Perhaps they thought this would work because they read a recent paper by Kühnen, et al. suggesting an epigenetic explanation for the "missing heritability" problem in obesity. Come by tomorrow morning (10.30h, BG7) to discuss:

Kühnen P, et al. [Interindividual Variation in DNA Methylation at a Putative POMC Metastable Epiallele Is Associated with Obesity.](http://www.ncbi.nlm.nih.gov/pubmed/27568547) Cell Metab. 2016 Aug 24. pii: S1550-4131(16)30377-1.

([slides](https://drive.google.com/open?id=1cQpSccrZy0saDw-XWun7t4_RTqcgHPbO1a6o5Hcsf6o))

# August 23, 2016

**Presenter**: Lotte Houtepen ([lotte.houtepen@bristol.ac.uk](mailto:lotte.houtepen@bristol.ac.uk))

Twins have been important to epigenetics for a long time. The oldest paper about both topics on pubmed was published in Science in 1978.

Wilson RS. Synchronies in mental development: an epigenetic perspective. Science. 1978 Dec 1;202(4371):939-48.

Here the author invokes 'epigenetics' to explain how initially discordant MZ twins become more concordant through development. Think about that: epigenetics is normally invoked to explain individual variation, not concordance. Even more interestingly, his comments about this seem to foreshadow discovery of an epigenetic clock:

"[This] would seem to argue for a powerful age-linked epigenetic determination of mental development."

At journal club tomorrow (10.30h in BG7), Lotte Houtepen will present the latest results about DNA methylation and aging in, yes, a twin study:

Tan Q, Heijmans BT, Hjelmborg JV, Soerensen M, Christensen K, Christiansen L.  
[Epigenetic drift in the aging genome: a ten-year follow-up in an elderly twin cohort.](http://www.ncbi.nlm.nih.gov/pubmed/27498152)  
Int J Epidemiol. 2016 Aug 6. pii: dyw132.

# August 16, 2016

**Presenter**: Matthew Suderman ([matthew.suderman@bristol.ac.uk](mailto:matthew.suderman@bristol.ac.uk))

According to [http://www.changemyface.com](http://www.changemyface.com/), this is what I would look like if I took up smoking:



Someone call 999.

At journal club tomorrow (10.30h in BG7), I will present analogous findings for the effects of stressful events on epigenetic age -- sorry, no scarry photos. Fortunately, there is more than just associations to report, there is evidence that age acceleration may be driven by stress hormones:

Zannas AS, Arloth J, Carrillo-Roa T, Iurato S, Röh S, Ressler KJ, Nemeroff CB, Smith AK, Bradley B, Heim C, Menke A, Lange JF, Brückl T, Ising M, Wray NR, Erhardt A, Binder EB, Mehta D. [Lifetime stress accelerates epigenetic aging in an urban, African American cohort: relevance of glucocorticoid signaling.](http://www.ncbi.nlm.nih.gov/pubmed/26673150) Genome Biol. 2015 Dec 17;16:266

([slides](https://drive.google.com/open?id=1RU_6uPCBYrZzZ5yWAmDFSgd_9Lfu3rDnIU0tMF19im0))

# August 9, 2016

**Presenter**: Doretta Caramaschi ([d.Caramaschi@bristol.ac.uk](mailto:d.Caramaschi@bristol.ac.uk))  
  
Montano, et al. [Association of DNA Methylation Differences With Schizophrenia in an Epigenome-Wide Association Study](http://www.ncbi.nlm.nih.gov/pubmed/27074206). JAMA Psychiatry. 2016 May 1;73(5):506-14.

# August 2, 2016

**Presenter**: Laurence Howe ([lh14833@bristol.ac.uk](mailto:lh14833@bristol.ac.uk))  
  
Minster, et al. [A thrifty variant in CREBRF strongly influences body mass index in Samoans](http://www.ncbi.nlm.nih.gov/pubmed/27455349). Nat Genet. 2016 Jul 25.

# July 26, 2016

**Presenter:** Gemma Sharp ([gemma.sharp@bristol.ac.uk](mailto:gemma.sharp@bristol.ac.uk))

Did you know that:

* 'Fetal alcohol spectrum disorder' is not a thing. It should be pluralized because it refers to a collection of disorders. In spite of this, it has its very own abbreviation FASD which is pluralized as FASDs (<http://www.cdc.gov/ncbddd/fasd/diagnosis.html>).
* People with FASDs can suffer for years with these disorders without knowing the cause because diagnosis is really not straight-forward (<http://www.cdc.gov/ncbddd/fasd/stories.html>).
* Our very own PC Haycock wrote a single-author review about the relevance of epigenetics to FASDs, and he used the right term! (<http://www.biolreprod.org/content/81/4/607.abstract>)

Tomorrow morning at 10:30 in BG7, Gemma Sharp will give us a guided tour through the latest investigation of DNA methylation and FASDs:

Portales-Casamar, et al. [DNA methylation signature of human fetal alcohol spectrum disorder](http://www.ncbi.nlm.nih.gov/pubmed/27358653). Epigenetics Chromatin. 2016 Jun 29;9:25.

# July 19, 2016

**Presenter:** Matthew Suderman ([matthew.suderman@bristol.ac.uk](mailto:matthew.suderman@bristol.ac.uk))

When Michael Gove said “**I think people in this country have had enough of experts**” he was of course referring to Ewan Birney, George Davey Smith and John Greally, and yet they still went ahead with their publication.

Come by tomorrow morning at 10:30 in BG7 if you'd like to hear about improving the interpretability of EWAS. I expect to see no more than 48% of you.

Birney E, Smith GD, Greally JM.  
[Epigenome-wide Association Studies and the Interpretation of Disease -Omics.](http://www.ncbi.nlm.nih.gov/pubmed/27336614)PLoS Genet. 2016 Jun 23;12(6):e1006105. doi: 10.1371/journal.pgen.1006105. eCollection 2016 Jun. Review. PMID: 27336614

([slides](https://docs.google.com/a/bristol.ac.uk/presentation/d/1huFxWWPVvlA274SMplpGIB7D2fgqgd0KnDDGahft--8/edit?usp=sharing))

# July 12, 2016

**Presenter:** Matthew Suderman ([matthew.suderman@bristol.ac.uk](mailto:matthew.suderman@bristol.ac.uk))

Tomorrow morning at 10:30 in BG7, there will be [bacon](https://bioconductor.org/packages/release/bioc/html/bacon.html).

Need I say more? Given the international reputation of bacon as a tasty gateway to a carnivorous diet, it should come as no surprise that bacon may be the ingredient every EWAS pipeline needs to counteract the bitter effects of inflation and bias.

Maarten M. van Iterson, Erik W. van Zwet, The Bios Consortium, P. Eline Slagboom, Bastiaan T. Heijmans. [Controlling bias and inflation in epigenome- and transcriptome-wide association studies using the empirical null distribution](http://biorxiv.org/content/early/2016/05/27/055772).

<http://biorxiv.org/content/early/2016/05/27/055772>

([slides](https://drive.google.com/open?id=1xm1rFK7eBFuRwwgdYywVJsFPqhYL3-DR7XQ-7qfICB8))

# July 5, 2016

**Presenter:** Lotte Houtepen ([lotte.houtepen@bristol.ac.uk](mailto:lotte.houtepen@bristol.ac.uk))

"Everything that irritates us about others can lead us to an understanding of ourselves."

-Carl Jung

Tomorrow morning at 10:30 in BG7, Lotte Houtepen will add that this could be our DNA methylation:

Houtepen LC, et al. [Genome-wide DNA methylation levels and altered cortisol stress reactivity following childhood trauma in humans](http://www.ncbi.nlm.nih.gov/pubmed/26997371). Nat Commun. 2016 Mar 21;7:10967. doi: 10.1038/ncomms10967.

# June 28, 2016

**Presenter:** Kim Burrows ([Kimberley.Burrows@bristol.ac.uk](mailto:Kimberley.Burrows@bristol.ac.uk))

As you step into the forest, your arm brushes a thorn. A drop of blood slides off your arm and hits the ground. Instantly, the forest senses a stranger, an atopic raised indoors.

Tomorrow morning at 10:30 in BG7, Kim Burrows will tell us more about this forest and how others can be grown using DNA methylation profiles:

Everson TM, Lyons G, Zhang H, Soto-Ramírez N, Lockett GA, Patil VK, Merid SK, Söderhäll C, Melén E, Holloway JW, Arshad SH, Karmaus W. [DNA methylation loci associated with atopy and high serum IgE: a genome-wide application of recursive Random Forest feature selection.](http://www.ncbi.nlm.nih.gov/pubmed/26292806) Genome Med. 2015 Aug 21;7:89. doi: 10.1186/s13073-015-0213-8.

# June 14, 2016

**Presenter**: Matthew Suderman ([matthew.suderman@bristol.ac.uk](mailto:matthew.suderman@bristol.ac.uk))

So you thought we knew how to best handle cell-type heterogeneity in an EWAS. Well time to think again! Even Houseman would be surprised by the paper I will present tomorrow at 10:30-11 in BG7:

McGregor K, Bernatsky S, Colmegna I, Hudson M, Pastinen T, Labbe A, Greenwood CM.  
[An evaluation of methods correcting for cell-type heterogeneity in DNA methylation studies.](http://www.ncbi.nlm.nih.gov/pubmed/27142380)  
Genome Biol. 2016 May 3;17(1):84. doi: 10.1186/s13059-016-0935-y.

([slides](https://drive.google.com/open?id=1QbU-mb0c9ourLpdTT2KBisARdj3I6rwgtE6Hx3gOC1I))

# June 7, 2016

**Presenter**: Matthew Suderman ([matthew.suderman@bristol.ac.uk](mailto:matthew.suderman@bristol.ac.uk))

No, air pollution is not full of sugar, and yet some claim that it raises blood glucose levels. Even more crazy, the paper I'll present tomorrow claims that the effect is partially mediated by DNA methylation. See you tomorrow at 10:30-11 in BG7:

Peng C, Bind MC, Colicino E, Kloog I, Byun HM, Cantone L, Trevisi L, Zhong J, Brennan K, Dereix AE, Vokonas PS, Coull BA, Schwartz JD, Baccarelli AA.  
[Particulate Air Pollution and Fasting Blood Glucose in Non-Diabetic Individuals: Associations and Epigenetic Mediation in the Normative Aging Study, 2000-2011.](http://www.ncbi.nlm.nih.gov/pubmed/27219535)Environ Health Perspect. 2016 May 24.

([slides](https://drive.google.com/open?id=1dBx7xwxzS8bwHmNHF2gj5Ajb4DSapOM758OwH1WHCYI))

# May 31, 2016

**Presenter**: Matthew Suderman ([matthew.suderman@bristol.ac.uk](mailto:matthew.suderman@bristol.ac.uk))

I was recently asked to add version numbers to [meffil](https://github.com/perishky/meffil) (an R package for analyzing DNA methylation data) so that users would know which set of bugs they might encounter. Previously this had just been a fun surprise, but, as we at meffil have learned, users don't like fun.

Apparently, our bodies agree, since DNA replication appears to come complete with a genetic versioning system. At the moment we're not sure if it tracks age as precisely as the epigenetic system but that may change.

Tomorrow morning at 10:30-11 in BG7, I will present the following paper (thanks to George Davey-Smith for sending it):

Alexandrov LB, Jones PH, Wedge DC, Sale JE, Campbell PJ, Nik-Zainal S, Stratton MR. [Clock-like mutational processes in human somatic cells.](http://www.ncbi.nlm.nih.gov/pubmed/26551669) Nat Genet. 2015 Dec;47(12):1402-7. doi: 10.1038/ng.3441. Epub 2015 Nov 9. PMID: 26551669

([slides](https://drive.google.com/open?id=1OhnMgZRd2gfs9Qt9McgTUKFenxWD7RaUHV7S_2PMnB4))

# May 24, 2016

**Presenter**: Anna Guyatt ([anna.guyatt@bristol.ac.uk](mailto:anna.guyatt@bristol.ac.uk))

Tomorrow morning at 10:30-11 in BG7, Anna Guyatt is going to tell us that being taller and thinner causes people to attain higher education levels and make more money. "How unfair!" I can hear you saying. Fortunately the IEU has you covered, one of these will be arriving shortly (pun intended):

<https://drive.google.com/open?id=0B-peG00QorQjQ0c5ckFfelluYjA>

In the meantime, Anna will help us to assess the evidence. In this case, the effect sizes will definitely not be ignored as they are given in British pounds.

Tyrrell, et al. [Height, body mass index, and socioeconomic status: mendelian randomisation study in UK Biobank.](http://www.ncbi.nlm.nih.gov/pubmed/26956984)

BMJ. 2016 Mar 8;352:i582. doi: 10.1136/bmj.i582.

PMID: 26956984

(George and Neil have written an editorial: <http://www.bmj.com/content/bmj/352/bmj.i1224.full.pdf>)

# May 17, 2016

**Presenter**: Rebecca Richmond ([Rebecca.Richmond@bristol.ac.uk](mailto:Rebecca.Richmond@bristol.ac.uk))

Tuesday morning at 10:30-11 in BG7, our very own Rebecca Richmond will be taking apart, piece by piece, a recent article by Siddhartha Mukherjee in The New Yorker:

Siddhartha Mukherjee. [Same but Different: How epigenetics can blur the line between nature and nurture](http://www.newyorker.com/magazine/2016/05/02/breakthroughs-in-epigenetics). The New Yorker, May 2016.

- Yes, *that* journal with impact factor in the hundreds.

- Yes, *that* author who won the 2011 Pulitzer Prize for nonfiction for “The Emperor of All Maladies: A Biography of Cancer".

# May 10, 2016

**Presenter**: Matthew Suderman ([matthew.suderman@bristol.ac.uk](mailto:matthew.suderman@bristol.ac.uk))

A couple of weeks ago it seemed like we might have cleared up the relationship between DNA methylation and gene expression. Well, not so fast. Those results were driven by an artificial system that permitted perturbation of a single gene. Tomorrow morning I will describe results from a set of set of real rat neurons that will once again show that nature is rarely simple.

See you tomorrow at 10:30-11:00 in BG7!

Hu Y, Huang K, An Q, Du G, Hu G, Xue J, Zhu X, Wang CY, Xue Z, Fan G.

Simultaneous profiling of transcriptome and DNA methylome from a single cell.

Genome Biol. 2016 May 5;17(1):88. doi: 10.1186/s13059-016-0950-z.

PMID: 27150361

([slides](https://drive.google.com/open?id=1FECyhy4sY3N7nw8bmOuWyHkfJrSL4OtCIkcnjICzk3E))

# May 3, 2016

**Presenter**: Matthew Suderman ([matthew.suderman@bristol.ac.uk](mailto:matthew.suderman@bristol.ac.uk))

Tomorrow morning (10:30-11:00 in BG7), I will give a brief overview of a paper comparing blood and saliva DNA methylation profiles of matched samples. A word of warning, this paper will not settle that question that has plaguing you the last year or two: would I have been able to publish in bigger journals if ARIES had saliva rather than blood DNA methylation profiles?

Jiang R, Jones MJ, Chen E, Neumann SM, Fraser HB, Miller GE, Kobor MS. [Discordance of DNA methylation variance between two accessible human tissues](http://www.ncbi.nlm.nih.gov/pubmed/25660083). Sci Rep. 2015 Feb 9;5:8257. doi: 10.1038/srep08257. PMID: 25660083

([slides](https://drive.google.com/open?id=1ViygKimuy1VEwR8qsFHXTQ4YnNMoipZbItuGtGBe15Q))

# April 19, 2016

**Presenter**: Matthew Suderman ([matthew.suderman@bristol.ac.uk](mailto:matthew.suderman@bristol.ac.uk))

A little epigenetic quiz for you:

Two transcriptional repressors wandered into a cell, DNMT3b and HDAC4 (actually they were transcribed there but that sounds less exciting):

1. Which is most likely to bump into an active EP53 gene transcriptional start site first?

2. How much will EP53 activity be repressed by each?

3. Which is most likely to provide lasting EP53 transcriptional repression after leaving the cell?

You should attend journal club tomorrow if:

1. You were unable to confidently answer all of these questions.

You clearly have not been keeping up with the literature, but this can be remedied in less than 30 minutes.

2. You confidently answered any these questions.

Aha! But EP53 is not a human gene. Although this level of ignorance cannot be remedied by a 30 minute journal club, it would make a great start.

Bintu, et al. [Dynamics of epigenetic regulation at the single-cell level](http://www.ncbi.nlm.nih.gov/pubmed/26912859). Science. 2016 Feb 12;351(6274):720-4.

([slides](https://drive.google.com/open?id=1QYuNQ9i6C8U2zJzuojDbhhQ9pd7_S-V1we6zyzg-B_I))

# April 12, 2016

**Presenter:** Hannah Elliott ([hannah.elliott@bristol.ac.uk](mailto:hannah.elliott@bristol.ac.uk))

Koestler DC, Jones MJ, Usset J, Christensen BC, Butler RA, Kobor MS, Wiencke JK, Kelsey KT. [Improving cell mixture deconvolution by identifying optimal DNA methylation libraries (IDOL).](http://www.ncbi.nlm.nih.gov/pubmed/26956433) BMC Bioinformatics. 2016 Mar 8;17(1):120. doi: 10.1186/s12859-016-0943-7.

PMID: 26956433

([slides](https://drive.google.com/open?id=0B-peG00QorQjN0lhVy1ldzg0ZDQ))

# March 15, 2016

**Presenter**: Lavinia Paternoster ([L.Paternoster@bristol.ac.uk](mailto:L.Paternoster@bristol.ac.uk))

At the IEU, we strive to be integrative. Come to journal club tomorrow to find out how to do that even better.

Gusve, et al. [Integrative approaches for large-scale transcriptome-wide association studies.](http://www.ncbi.nlm.nih.gov/pubmed/26854917) Nat Genet. 2016 Mar;48(3):245-52. doi: 10.1038/ng.3506. Epub 2016 Feb 8.  
PMID: 26854917

# March 8, 2016

**Presenter**: James Jungius ([james.jungius@bristol.ac.uk](mailto:james.jungius@bristol.ac.uk))

If you were one of the good children, then you celebrated your mother yesterday and thanked her for eating broccoli, spinach and dried legumes so many years ago.

Tomorrow morning (10:30-11:00 in BG7), James Jungius will present:

Joubert, et al. [Maternal plasma folate impacts differential DNA methylation in an epigenome-wide meta-analysis of newborns.](http://www.ncbi.nlm.nih.gov/pubmed/26861414) Nat Commun. 2016 Feb 10;7:10577.

# March 1, 2016

**Presenter**: Matthew Suderman ([matthew.suderman@bristol.ac.uk](mailto:matthew.suderman@bristol.ac.uk))

The **obesity** epidemic: **explained** -- well not really but here is one hypothesis based on an animal model and some suggestive human data.

Tomorrow morning (10:30-11:00 in BG7), I will present the following:

Dalgaard, et al. [Trim28 Haploinsufficiency Triggers Bi-stable Epigenetic Obesity.](http://www.ncbi.nlm.nih.gov/pubmed/26824653)

Cell. 2016 Jan 28;164(3):353-64.

([slides](https://drive.google.com/open?id=1Z6o49sozA1QJZZaEC0R2-Yp0rmixt1WIVHf8ui_efJc))

# February 23, 2016

**Presenter**: Josine Min (josine.min[@bristol.ac.uk](mailto:Rebecca.Richmond@bristol.ac.uk))

What can we learn from:

43 twins

adipose tissue samples

blood samples

whole-genome DNA methylation profiles (30 million CpG sites, not 450K!)

Tomorrow morning (10:30-11:00 in BG7) Josine Min will present the highlights:

Busche, et al. [Population whole-genome bisulfite sequencing across two tissues highlights the environment as the principal source of human methylome variation.](http://www.ncbi.nlm.nih.gov/pubmed/26699896) Genome Biol. 2015 Dec 23;16(1):290.

[slides](https://drive.google.com/open?id=0B4u5WFRyVgbzb0YwUFdQcmVJM28)

# February 16, 2016

**Presenter**: Rebecca Richmond ([Rebecca.Richmond@bristol.ac.uk](mailto:Rebecca.Richmond@bristol.ac.uk))

Tomorrow morning (10:30-11:00 in BG7) join us in guessing each others genotypes!

Rebecca Richmond will present:

Hu, et al. [GWAS of 89,283 individuals identifies genetic variants associated with self-reporting of being a morning person.](http://www.nature.com/ncomms/2016/160202/ncomms10448/full/ncomms10448.html) Nat Commun. 2016 Feb 2;7:10448.

Along with the accompanying UKBiobank working papers (<http://biorxiv.org/content/early/2016/02/02/031369?rss=1> and<http://biorxiv.org/content/early/2016/02/02/038620>)

# February 2, 2016

**Presenter**: Matthew Suderman ([matthew.suderman@bristol.ac.uk](mailto:matthew.suderman@bristol.ac.uk))

Clearly, any name that contains "super" must be important (would "suder" be close enough?).

Heyn et al. [Epigenomic analysis detects aberrant super-enhancer DNA methylation in human cancer.](http://www.ncbi.nlm.nih.gov/pubmed/26813288) Genome Biol. 2016 Jan 26;17(1):11.

([slides](https://docs.google.com/a/bristol.ac.uk/presentation/d/1rj326-1yGY6VY5kpJ-npKx9IgpZwLcQPRnjv4uXufSA/edit?usp=sharing))

# January 26, 2016

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**Presenter:**  Diana Juvinao ([diana.juvinao-quintero@bristol.ac.uk](mailto:diana.juvinao-quintero@bristol.ac.uk))

Chambers, et al. [Epigenome-wide association of DNA methylation markers in peripheral blood from Indian Asians and Europeans with incident type 2 diabetes: a nested case-control study.](http://www.ncbi.nlm.nih.gov/pubmed/26095709) Lancet Diabetes Endocrinol. 2015 Jul;3(7):526-34.

([paper](https://drive.google.com/open?id=0B-peG00QorQjUFB3VmdFR0tYUUU); [slides](https://drive.google.com/open?id=0B-peG00QorQjbTJpNDdVTWZxd1E))

# January 19, 2016

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**Presenter:** Katherine Tansey ([katherine.tansey@bristol.ac.uk](mailto:katherine.tansey@bristol.ac.uk))

Finucane, et al. [Partitioning heritability by functional annotation using genome-wide association summary statistics](http://www.ncbi.nlm.nih.gov/pubmed/26414678). Nat Genet. 2015 Nov;47(11):1228-35.

([slides](https://drive.google.com/open?id=0B-peG00QorQjZFRpOGF0cmxTWDQzcVZaZk5ncFNNQzFaTXM0))

# January 12, 2016

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**Presenter:** Gemma Sharp ([gemma.sharp@bristol.ac.uk](mailto:gemma.sharp@bristol.ac.uk))

Wang S, Song J, Yang Y, Zhang Y, Wang H, Ma J. [HIF3A DNA Methylation Is Associated with Childhood Obesity and ALT.](http://www.ncbi.nlm.nih.gov/pubmed/26717317) PLoS One. 2015 Dec 30;10(12):e0145944.

This will include an update on the work that she, Rebecca Richmond and Mary Ward have submitted on HIF3A methylation and childhood BMI.

# December 15, 2015

**Presenter**: Josine Min ([Josine.Min@bristol.ac.uk](mailto:Josine.Min@bristol.ac.uk))

Trynka G, Westra HJ, Slowikowski K, Hu X, Xu H, Stranger BE, Klein RJ, Han B, Raychaudhuri S. [Disentangling the Effects of Colocalizing Genomic Annotations to Functionally Prioritize Non-coding Variants within Complex-Trait Loci.](http://www.ncbi.nlm.nih.gov/pubmed/26140449) Am J Hum Genet. 2015 Jul 2;97(1):139-52. doi: 10.1016/j.ajhg.2015.05.016.

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# December 8, 2015

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**Presenter:** Katherine Tansey ([katherine.tansey@bristol.ac.uk](mailto:katherine.tansey@bristol.ac.uk))

Bulik-Sullivan et al. An atlas of genetic correlations across human diseases and traits. Nat Genet. 2015 Nov;47(11):1236-41.

([slides](https://drive.google.com/open?id=0B-peG00QorQjV1RSRFdfSXpNUXhMdEdvRTBnNTAyNEVWbXdR))

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# November 24, 2015

**Presenter**: Laura Corbin ([laura.corbin@bristol.ac.uk](mailto:laura.corbin@bristol.ac.uk))

Part II of Claussnitzer, et al.

# November 17, 2015

**Presenter**: Lavinia Paternoster ([L.Paternoster@bristol.ac.uk](mailto:L.Paternoster@bristol.ac.uk))

Claussnitzer M, Dankel SN, Kim KH, Quon G, Meuleman W, Haugen C, Glunk V, Sousa IS, Beaudry JL, Puviindran V, Abdennur NA, Liu J, Svensson PA, Hsu YH, Drucker DJ, Mellgren G, Hui CC, Hauner H, Kellis M. [FTO Obesity Variant Circuitry and Adipocyte Browning in Humans.](http://www.ncbi.nlm.nih.gov/pubmed/26287746)

N Engl J Med. 2015 Sep 3;373(10):895-907.

<http://www.nejm.org/doi/full/10.1056/NEJMoa1502214>

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# November 10, 2015

**Presenter:** Hannah Elliott ([hannah.elliott@bristol.ac.uk](mailto:hannah.elliott@bristol.ac.uk))

Voisin S, Almén MS, Zheleznyakova GY, Lundberg L, Zarei S, Castillo S, Eriksson FE, Nilsson EK, Blüher M, Böttcher Y, Kovacs P, Klovins J, Rask-Andersen M, Schiöth HB. [Many obesity-associated SNPs strongly associate with DNA methylation changes at proximal promoters and enhancers.](http://www.ncbi.nlm.nih.gov/pubmed/26449484) Genome Med. 2015 Oct 8;7(1):103.

([slides](https://drive.google.com/open?id=0B-peG00QorQjenE5QXJJUktsdWhQSXZJeVIwTjl6RlJpT3ow))

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# November 3, 2015

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**Presenter:** Katherine Tansey ([katherine.tansey@bristol.ac.uk](mailto:katherine.tansey@bristol.ac.uk))

Bulik-Sullivan BK, Loh PR, Finucane HK, Ripke S, Yang J; Schizophrenia Working Group of the Psychiatric Genomics Consortium, Patterson N, Daly MJ, Price AL, Neale BM. [LD Score regression distinguishes confounding from polygenicity in genome-wide association studies.](http://www.ncbi.nlm.nih.gov/pubmed/25642630) Nat Genet. 2015 Mar;47(3):291-5.

([slides](https://drive.google.com/open?id=0B-peG00QorQjMnNxdllpcDNyeTg))

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# October 27, 2015

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**Presenter:** Kim Burrows ([Kimberley.Burrows@bristol.ac.uk](mailto:Kimberley.Burrows@bristol.ac.uk))

Kato, et al. [Trans-ancestry genome-wide association study identifies 12 genetic loci influencing blood pressure and implicates a role for DNA methylation](http://www.ncbi.nlm.nih.gov/pubmed/26390057). Nat Genet. 2015 Nov;47(11):1282-93. doi: 10.1038/ng.3405.

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# October 20, 2015

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**Presenter:** Dan Lawson ([Dan.Lawson@bristol.ac.uk](mailto:Dan.Lawson@bristol.ac.uk))

Llorente MG, Jones ER, Eriksson A, Siska V, Arthur KW, Arthur JW, Curtis MC, Stock JT, Coltorti M, Pieruccini P, Stretton S, Brock F, Higham T, Park Y, Hofreiter M, Bradley DG, Bhak J, Pinhasi R, Manica A. [Ancient Ethiopian genome reveals extensive Eurasian admixture throughout the African continent.](http://www.ncbi.nlm.nih.gov/pubmed/26449472) Science. 2015 Oct 8.

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# October 13, 2015

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**Presenter:** Gemma Sharp ([gemma.sharp@bristol.ac.uk](mailto:gemma.sharp@bristol.ac.uk))

Florath I, Butterbach K, Heiss J, Bewerunge-Hudler M, Zhang Y, Schöttker B, Brenner H. [Type 2 diabetes and leukocyte DNA methylation: an epigenome-wide association study in over 1,500 older adults](http://www.ncbi.nlm.nih.gov/pubmed/26433941). Diabetologia. 2015 Oct 3.

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# October 6, 2015

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**Presenter:** Rebecca Richmond ([Rebecca.Richmond@bristol.ac.uk](mailto:Rebecca.Richmond@bristol.ac.uk))

Teschendorff, et al. [Correlation of Smoking-Associated DNA Methylation Changes in Buccal Cells With DNA Methylation Changes in Epithelial Cancer](http://www.ncbi.nlm.nih.gov/pubmed/26181258). JAMA Oncol. 2015 Jul;1(4):476-85.

# September 29, 2015

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**Presenter:** Matthew Suderman ([matthew.suderman@bristol.ac.uk](mailto:matthew.suderman@bristol.ac.uk))

Fortin JP, Hansen KD. [Reconstructing A/B compartments as revealed by Hi-C using long-range correlations in epigenetic data.](http://www.ncbi.nlm.nih.gov/pubmed/26316348) Genome Biol. 2015 Aug 28;16(1):180.

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# September 22, 2015

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**Presenter:** Gibran Hemani ([g.hemani@bristol.ac.uk](mailto:g.hemani@bristol.ac.uk))

Yang, et al. [Genetic variance estimation with imputed variants finds negligible missing heritability for human height and body mass index.](http://www.ncbi.nlm.nih.gov/pubmed/26323059) Nat Genet. 2015 Aug 31. doi: 10.1038/ng.3390.

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# September 8, 2015

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**Presenter:** Matthew Suderman ([matthew.suderman@bristol.ac.uk](mailto:matthew.suderman@bristol.ac.uk))

Hasegawa Y, Taylor D, Ovchinnikov DA, Wolvetang EJ, de Torrenté L, Mar JC.

[Variability of Gene Expression Identifies Transcriptional Regulators of Early Human Embryonic Development.](http://www.ncbi.nlm.nih.gov/pubmed/26288249) PLoS Genet. 2015 Aug 19;11(8):e1005428.

([slides](https://drive.google.com/open?id=1YC6y75RTctCZQwXIlTI_ougJ0Fd_pMGMvYg3RiplzQw))

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# August 25, 2015

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**Presenter:** Matthew Suderman ([matthew.suderman@bristol.ac.uk](mailto:matthew.suderman@bristol.ac.uk))

Tang et al. [A Unique Gene Regulatory Network Resets the Human Germline Epigenome for Development](http://www.ncbi.nlm.nih.gov/pubmed/26046444). Cell. 2015 Jun 4;161(6):1453-67. doi: 10.1016/j.cell.2015.04.053. PMID: 26046444.

([slides](https://docs.google.com/a/bristol.ac.uk/presentation/d/1ltDFZHUIbvQZxedpdwf9vGbG4G59zYn4Ifusl0SPsyU/edit?usp=sharing))

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# August 18, 2015

**Presenter:** Gemma Sharp ([gemma.sharp@bristol.ac.uk](mailto:gemma.sharp@bristol.ac.uk))

Burris, Baccarelli, Byun, Cantoral, Just et al. O[ffspring DNA methylation of the aryl-hydrocarbon receptor repressor gene is associated with maternal BMI, gestational age, and birth weight](http://www.tandfonline.com/doi/full/10.1080/15592294.2015.1078963#abstract). Epigenetics. 2015 Aug 7; PMID: 26252179

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# August 11, 2015

**Presenter:** Gemma Sharp ([gemma.sharp@bristol.ac.uk](mailto:gemma.sharp@bristol.ac.uk))

Shah S, Bonder MJ, Marioni RE, ... Deary IJ, Visscher PM. [Improving Phenotypic Prediction by Combining Genetic and Epigenetic Associations](http://www.sciencedirect.com/science/article/pii/S0002929715002001). Am J Hum Genet. 2015 Jul 2;97(1):75-85 PMID: 26119815

([slides](https://drive.google.com/file/d/0B9wV5QepRlaWWTR0UEk3a2hxRjg/view?usp=sharing))

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# August 4, 2015

**Presenter:** Gibran Hemani ([g.hemani@bristol.ac.uk](mailto:g.hemani@bristol.ac.uk))

Ernst J, Kellis M. [Large-scale imputation of epigenomic datasets for systematic annotation of diverse human tissues.](http://www.ncbi.nlm.nih.gov/pubmed/25690853) Nat Biotechnol. 2015 Apr;33(4):364-76. doi: 10.1038/nbt.3157. Epub 2015 Feb 18. PMID: 25690853

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# July 28, 2015

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**Presenter:** Matthew Suderman ([matthew.suderman@bristol.ac.uk](mailto:matthew.suderman@bristol.ac.uk))

Miller GE, Yu T, Chen E, Brody GH.

[Self-control forecasts better psychosocial outcomes but faster epigenetic aging in low-SES youth.](http://www.ncbi.nlm.nih.gov/pubmed/26170291) Proc Natl Acad Sci U S A. 2015 Jul 13. PMID: 26170291

([slides](https://drive.google.com/open?id=1Oh0QSQQT9ri01sJgMg4RQTR1aU4Q9fYu6fLLHqRkg28))

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# July ~~14~~21, 2015

**Presenter:** Matthew Suderman ([matthew.suderman@bristol.ac.uk](mailto:matthew.suderman@bristol.ac.uk))

Gutierrez-Arcelus, et al.

[Tissue-specific effects of genetic and epigenetic variation on gene regulation and splicing.](http://www.ncbi.nlm.nih.gov/pubmed/25634236)

PLoS Genet. 2015 Jan 29;11(1):e1004958. doi: 10.1371/journal.pgen.1004958.

PMID: 25634236

([slides](https://drive.google.com/open?id=1WGkqFNRROVh3mZoIeyJTiDHhJdgNn2awn_wC72YxcS4))

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# July 7, 2015

**Presenter:** Matthew Suderman ([matthew.suderman@bristol.ac.uk](mailto:matthew.suderman@bristol.ac.uk))

Gutierrez-Arcelus et al.

[Passive and active DNA methylation and the interplay with genetic variation in gene regulation.](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3673336/)

Elife. 2013 Jun 4;2:e00523. doi: 10.7554/eLife.00523.

PMID: 23755361

([slides](https://drive.google.com/open?id=1YhvOAQIfwUO-5h_HyVIdLn_gDojI8YCNiYKP4fMi-fg))

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# June 23 and 30, 2015

No meeting as we’ll all be at the following conference:

Mendelian randomization: From population health to pharmaceutical development.

(<http://www.mendelianrandomization.org.uk/>).

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# June 16, 2015

**Presenter:** Gemma Sharp ([gemma.sharp@bristol.ac.uk](mailto:gemma.sharp@bristol.ac.uk))

[Childhood maternal care is associated with DNA methylation of the genes for brain-derived neurotrophic factor (BDNF) and oxytocin receptor (OXTR) in peripheral blood cells in adult men and women.](http://www.ncbi.nlm.nih.gov/pubmed/26061800) Unternaehrer E, Meyer AH, Burkhardt SC, Dempster E, Staehli S, Theill N, Lieb R, Meinlschmidt G. Stress. 2015 Jun 10:1-11.

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# June 9, 2015

**Presenter:** Matthew Suderman ([matthew.suderman@bristol.ac.uk](mailto:matthew.suderman@bristol.ac.uk))

[Human body epigenome maps reveal noncanonical DNA methylation variation.](http://www.ncbi.nlm.nih.gov/pubmed/26030523)

Schultz MD, He Y, Whitaker JW, Hariharan M, Mukamel EA, Leung D, Rajagopal N, Nery JR, Urich MA, Chen H, Lin S, Lin Y, Jung I, Schmitt AD, Selvaraj S, Ren B, Sejnowski TJ, Wang W, Ecker JR.

Nature. 2015 Jun 1. doi: 10.1038/nature14465.

([slides](https://drive.google.com/open?id=0B-peG00QorQjVmJxVEZCSVU0alE&authuser=0))

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# June 2, 2015

**Presenter:** Matthew Suderman ([matthew.suderman@bristol.ac.uk](mailto:matthew.suderman@bristol.ac.uk))

[Understanding multicellular function and disease with human tissue-specific networks.](http://www.ncbi.nlm.nih.gov/pubmed/25915600)

Greene CS, Krishnan A, Wong AK, Ricciotti E, Zelaya RA, Himmelstein DS, Zhang R, Hartmann BM, Zaslavsky E, Sealfon SC, Chasman DI, FitzGerald GA, Dolinski K, Grosser T, Troyanskaya OG.

Nat Genet. 2015 Jun;47(6):569-76. doi: 10.1038/ng.3259. Epub 2015 Apr 27.

PMID: 25915600

([slides](https://drive.google.com/open?id=0B-peG00QorQjN2sxWTlIRFMyMHM&authuser=0))

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# May 26, 2015

**Presenter:** Matthew Suderman ([matthew.suderman@bristol.ac.uk](mailto:matthew.suderman@bristol.ac.uk))

[Effects of Particulate Matter Exposure on Blood 5-hydroxymethylation: Results from the Beijing Truck Driver Air Pollution Study.](http://www.ncbi.nlm.nih.gov/pubmed/25970091)

Sanchez-Guerra M, Zheng Y, Osorio-Yanez C, Zhong J, Chervona Y, Wang S, Chang D, McCracken JP, Díaz A, Bertazzi PA, Koutrakis P, Kang CM, Zhang X, Zhang W, Byun HM, Schwartz J, Hou L, Baccarelli AA.

Epigenetics. 2015 May 13:0. PMID: 25970091

([pdf](https://drive.google.com/open?id=0B-peG00QorQjU0F4S0RVeWZYVkE&authuser=0))

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# May 12, 2015

In lieu of next week's Epigenetics Journal Club, we're lucky to have a presentation from Stig Egil Bojesen from the University of Copenhagen, who will be talking about his work on DNA methylation and cancer. Stig is a consultant and researcher based in the Institute for Clinical Medicine at the University of Copenhagen. His main interest is in cancer genetics and much of his research involves participants of the Copenhagen City Heart Study and the Copenhagen General Population Study. Stig will be presenting his work looking at the relationship between smoking, methylation at AHRR and cancer, in particular the development of a Taqman assay to measure methylation.

Stig's talk is from 10:00-11:00 in seminar room OS6, Tuesday 12th May.

<http://publichealth.ku.dk/staff/?pure=en%2Fpersons%2Fstig-egil-bojesen(25f871c8-a69d-45d1-85b6-c438d7293b74)%2Fpublications.html>

# May 5, 2015

**(12pm today only, room booking conflict)**

**Presenter:** Rebecca Richmond ([Rebecca.Richmond@bristol.ac.uk](mailto:Rebecca.Richmond@bristol.ac.uk))

[DNA methylation mediates the effect of maternal smoking during pregnancy on birthweight of the offspring.](http://www.ncbi.nlm.nih.gov/pubmed/25862628) Küpers LK, Xu X, Jankipersadsing SA, Vaez A, la Bastide-van Gemert S, Scholtens S, Nolte IM, Richmond RC, Relton CL, Felix JF, Duijts L, van Meurs JB, Tiemeier H, Jaddoe VW, Wang X, Corpeleijn E, Snieder H.

Int J Epidemiol. 2015 Apr 10. pii: dyv048.

PMID: 25862628

**Summary.** A small number of CpG sites strongly associated with tobacco exposure appear to mediate the effect of prenatal tobacco exposure on birthweight. The mediation effect cannot be explained away by the CpG sites simply being good proxies for tobacco exposure because the sites most strongly associated with the exposure do not appear to be mediators. The result was replicated in ARIES and Generation R, though in ARIES the effect was much weaker possibly due to the lower number of smoking mothers.

# April 28, 2015

**Presenter:** Gemma Sharp ([gemma.sharp@bristol.ac.uk](mailto:gemma.sharp@bristol.ac.uk))

[Whole genome bisulfite sequencing of cell-free DNA and its cellular contributors uncovers placenta hypomethylated domains.](http://www.ncbi.nlm.nih.gov/pubmed/25886572) Jensen TJ, Kim SK, Zhu Z, Chin C, Gebhard C, Lu T, Deciu C, van den Boom D, Ehrich M. Genome Biol. 2015 Apr 15;16(1):78. PMID: 25886572

**Summary.** Fetal DNA finds it’s way into circulating maternal blood through the placenta, providing a non-invasive means to study fetal DNA. Circulating DNA is a mixture of maternal and fetal DNA and currently only sequence characteristics have been used to determine identity. The authors wondered if methylation patterns of this DNA could be used to improve identification. They do not attempt to answer this question but instead report the ability to generate methylation profiles of circulating DNA of reasonable quality.

Circulating DNA from a small number pregnant and non-pregnant women as well as placental DNA was sequenced using whole genome bisulfite sequencing in order to generate genetic and methylation profiles. Longer fragments of circulating DNA typically had higher methylation levels. Placental DNA methylation is hypomethylated compared to both pregnant and non-pregnant circulating DNA, particularly in large regions of low CpG and gene density.

# April 21, 2015

**Presenter**: Josine Min ([Josine.Min@bristol.ac.uk](mailto:Josine.Min@bristol.ac.uk))

[Integrative analysis of 111 reference human epigenomes.](http://www.ncbi.nlm.nih.gov/pubmed/25693563)

Roadmap Epigenomics Consortium, et al.

Nature. 2015 Feb 19;518(7539):317-30.

**Summary.** Part II from March 24. This paper describes the analysis of histone modification, DNA accessibility, DNA methylation and RNA expression profiles from 111 human samples. From these they “establish global maps of regulatory elements, define regulatory modules of coordinated activity, and their likely activators and repressors.” They “show that disease- and trait-associated genetic variants are enriched in tissue-specific epigenomic marks” revealing cell-specificity of human traits and diseases.

# March 31, 2015

**Presenter**: Lavinia Paternoster ([L.Paternoster@bristol.ac.uk](mailto:L.Paternoster@bristol.ac.uk))

[An epigenome-wide association study of total serum immunoglobulin E concentration.](http://www.ncbi.nlm.nih.gov/pubmed/25707804)

Liang L, Willis-Owen SA, Laprise C, Wong KC, Davies GA, Hudson TJ, Binia A, Hopkin JM, Yang IV, Grundberg E, Busche S, Hudson M, Rönnblom L, Pastinen TM, Schwartz DA, Lathrop GM, Moffatt MF, Cookson WO.

Nature. 2015 Feb 18.

**Summary.** Identify a large number of CpG sites strongly associated with immunoglobulin E concentration in blood. However, most associations are significantly weakened when eosinophil concentrations are included.

**Follow-up.** The associations can be replicated in ARIES but again eosinophil concentrations are important.

# March 24, 2015

**Presenter**: Josine Min ([Josine.Min@bristol.ac.uk](mailto:Josine.Min@bristol.ac.uk))

[Integrative analysis of 111 reference human epigenomes.](http://www.ncbi.nlm.nih.gov/pubmed/25693563)

Roadmap Epigenomics Consortium, et al.

Nature. 2015 Feb 19;518(7539):317-30.

**Summary.** Long paper. We will finish it in another session.

# March 3/10/17, 2015

No meetings as most of us will be away.

# February 24, 2015

**Presenter:** Matthew Suderman ([matthew.suderman@bristol.ac.uk](mailto:matthew.suderman@bristol.ac.uk))

[Epigenomic analysis of primary human T cells reveals enhancers associated with TH2 memory cell differentiation and asthma susceptibility.](http://www.ncbi.nlm.nih.gov/pubmed/24997565)

Seumois G, Chavez L, Gerasimova A, Lienhard M, Omran N, Kalinke L, Vedanayagam M, Ganesan AP, Chawla A, Djukanović R, Ansel KM, Peters B, Rao A, Vijayanand P.

Nat Immunol. 2014 Aug;15(8):777-88.

**Summary.** H3K4me2 profiles were generated from isolated naive, TH1 and TH2 cells from the peripheral blood of healthy and asthmatic individuals. H3K4me2 profiles are reportedly the most precise and reliable means to identify active or poised enhancers. H3K4me2 differences between naive, TH1 and TH2 cells were identified (ignoring asthma) as well as differences between asthma and controls in all cell types. H3K4me2 differences were assumed to identify enhancers with differing levels of activity. Analysis of these differences involved testing these differentially methylated enhancers for enriched overlap with putative transcription factor binding sites identified both by binding motifs as well as from actual binding profiles generated by the [Roadmap Epigenomics Project](http://www.roadmapepigenomics.org). CTCF profiles from the same project were used to partition the genome into regulatory regions within which enhancers were assumed to play a role in the regulation of all genes. Analysis confirmed known differences between cell types. The vast majority of H3K4me2 differences between asthma and controls were found in TH2 cells, and these differences contained an unexpectedly large number of asthma associated single nucleotide polymorphisms (SNPs). These findings suggest that altered regulation of TH2 cell enhancers may mediate the pathogenic effects of many asthma associated SNPs.

# February 17, 2015

**Presenter:** Cathy Elks ([cathy.elks@bristol.ac.uk](mailto:cathy.elks@bristol.ac.uk))

[DNA methylation age of blood predicts all-cause mortality in later life.](http://www.ncbi.nlm.nih.gov/pubmed/25633388)

Marioni RE, Shah S, McRae AF, Chen BH, Colicino E, Harris SE, Gibson J, Henders AK, Redmond P, Cox SR, Pattie A, Corley J, Murphy L, Martin NG, Montgomery GW, Feinberg AP, Fallin M, Multhaup ML, Jaffe AE, Joehanes R, Schwartz J, Just AC, Lunetta KL, Murabito JM, Starr JM, Horvath S, Baccarelli AA, Levy D, Visscher PM, Wray NR, Deary IJ.

Genome Biol. 2015 Jan 30;16(1):25.

([slides](https://drive.google.com/open?id=0B-peG00QorQjNnd6WEZxeU9TZDlubHdfYUFhQ0xSN1lRbXM4&authuser=0))

**Summary:** DNA methylation levels in a variety of tissues can be used to accurately predict age. Predictions are not perfect so we call these estimates DNA methylation age. An attractive hypothesis is that DNA methylation age better estimates the true biological age of a person than chronological age. This study investigates whether or not accelerated DNA methylation age relative to chronological age might be associated increased all-cause mortality. The authors find that a 5-year higher DNA methylation age is associated with a 16% higher mortality risk. This association may be the result of both health and genetic factors because they also show that heritability of DNA methylation age acceleration is 0.43.

# February 10, 2015

No meeting this week since most of us will be away.

# February 3, 2015

**Presenter:** Hannah Elliott ([hannah.elliott@bristol.ac.uk](mailto:hannah.elliott@bristol.ac.uk))

[Epigenetic signatures of internal migration in Italy.](http://www.ncbi.nlm.nih.gov/pubmed/25324151)

Campanella G, Polidoro S, Di Gaetano C, Fiorito G, Guarrera S, Krogh V, Palli D, Panico S, Sacerdote C, Tumino R, Elliott P, Matullo G, Chadeau-Hyam M, Vineis P.

Int J Epidemiol. 2014 Oct 15. pii: dyu198.

([slides](https://drive.google.com/open?id=0B-peG00QorQjQUlaSk1nUDEzcENORlY1NExqSy1XbmtzQnBF&authuser=0))

**Summary:** The main focus of this cross sectional study was an EWAS using 450k arrays to identify differences in methylation between south to north migrants in Italy compared to their host (north western Italian) and origin (southern Italian) populations. Samples were drawn from EPIC-Italy. Beta regression models were used; in fully adjusted models there were no differences between migrant and origin populations but several differences in DNA methylation remained between migrant and host populations even after adjustment for diet and lifestyle measures available and after removing CpGs with multiple homology or near to SNPs. Of particular interest was a region on Chromosome 7 & the authors further analysed this region using PCA, showing the 1st and 15th components were associated with migration.

# January 27, 2015

**Presenter:** Gemma Sharp ([gemma.sharp@bristol.ac.uk](mailto:gemma.sharp@bristol.ac.uk))

[Adiposity is associated with DNA methylation profile in adipose tissue.](http://www.ncbi.nlm.nih.gov/pubmed/25541553)

Agha G, Houseman EA, Kelsey KT, Eaton CB, Buka SL, Loucks EB.

Int J Epidemiol. 2014 Dec 25. pii: dyu236.

([slides](https://drive.google.com/open?id=0B-peG00QorQjajdjM0t1ZlpyOUk&authuser=0))

**Summary:** The goal of this small study (106 middle age men and women) was “to evaluate whether genome-wide DNA methylation profiles in subcutaneous adipose tissue and peripheral blood leukocytes are associated with measures of adiposity”. Because of the small study size, statistical power was low so the authors utilized an omnibus test of significance, i.e. for each measure of adiposity, they compared the overall strength of associations with DNA methylation at each CpG site to some null distribution. The minimum CpG site p-value was used to summarize the overall strength, and the null distribution was generated by randomly permuting the adiposity measure 1000 times, each time recomputing association p-values between methylation levels and the permuted measure and identifying the minimum p-value. Significant associations were identified in adipose tissue but not in blood. This contrasts with cigarette smoking which appears to have significantly overlapping effects on a variety of tissues. The authors did not observe associations in blood at the three HIF3A CpG sites recently identified in a much larger study [(Dick et al. Lancet, 2014)](http://www.ncbi.nlm.nih.gov/pubmed/24630777).

# January 20, 2015

**Presenter:** Gibran Hemani ([g.hemani@bristol.ac.uk](mailto:g.hemani@bristol.ac.uk))

[Genetic and environmental exposures constrain epigenetic drift over the human life course.](http://www.ncbi.nlm.nih.gov/pubmed/25249537)

Shah S, McRae AF, Marioni RE, Harris SE, Gibson J, Henders AK, Redmond P, Cox SR, Pattie A, Corley J, Murphy L, Martin NG, Montgomery GW, Starr JM, Wray NR, Deary IJ, Visscher PM.

Genome Res. 2014 Nov;24(11):1725-33. doi: 10.1101/gr.176933.114. Epub 2014 Sep 23.

([slides](https://drive.google.com/open?id=0B-peG00QorQjMjAxRjVtQUUzMzQ&authuser=0) -- brought to you by [EVERNOTE](https://evernote.com/), *“the workspace for your life’s work”*)

**Summary:** Similarly to last week, the authors investigate the extent to which methylation levels change over time and how change is constrained. They use methylation profiles from the same individuals at two time points 6-10 years apart (Lothian Birth Cohorts of 1921 and 1936) to estimate repeatability at CpG sites, i.e. methylation variance over time divided by overall variance. They find that repeatability overall is much greater than expected at random (over 68% of probes have non-zero repeatability), so something is preventing methylation at these sites from changing randomly. One constraint is genetic since repeatability and methylation heritability is highly correlated (R2 = 0.68). Another constraint is environmental exposure since CpG sites associated with tobacco smoke exposure and sex tended to have higher than expected levels of repeatability.

# January 13, 2015

**Presenter:** Matthew Suderman ([matthew.suderman@bristol.ac.uk](mailto:matthew.suderman@bristol.ac.uk))

[Genome-wide DNA methylation variability in adolescent monozygotic twins followed since birth.](http://www.ncbi.nlm.nih.gov/pubmed/25437055)

Lévesque ML, Casey KF, Szyf M, Ismaylova E, Ly V, Verner MP, Suderman M, Brendgen M, Vitaro F, Dionne G, Boivin M, Tremblay RE, Booij L.

Epigenetics. 2014;9(10):1410-21. doi: 10.4161/15592294.2014.970060.

([pdf](https://drive.google.com/open?id=0B-peG00QorQjc3FpX3JZQjlCS1E&authuser=0); [slides](https://drive.google.com/open?id=1rPGF5Dv1Qf8S6TJOdgcfLDcG3DDE6ssnfD1t5woBtzc&authuser=0))

**Summary:** DNA methylation patterns are influenced by many factors, including environmental, genetic or developmental factors. Patterns that are not stable over short time periods or are genetically determined are unlikely to be informative of early life exposures. The authors identify CpG sites with methylation variance that is not genetically determined by comparing methylation profiles between monozygotic twin pairs. They identify sites that vary over short periods by comparing methylation profiles from the same individuals that were generated six months apart. The intersection of these two sets consistents of a very small number of CpG sites (258) that are likely of most interest to epigenetic studies of early life exposure.