# Alan P. Boyle

### **Education**

Doctor of Philosophy, Computational Biology and Bioinformatics Duke University, Durham, NC
 Bachelor of Science, Biochemistry and Molecular Biology Bachelor of Science, Computer Science Mississippi State University, Starkville, MS

## **Academic Appointments**

Assistant Professor, Department of Computational Medicine & Bioinformatics 2014-present Member, Program in Biomedical Sciences Member, Bioinformatics Training Program Assistant Professor, Department of Human Genetics 2015-present Member, Genome Science Training Program (GSTP) Member, Michigan Predoctoral Training Program in Genetics (GTP) Member, Center for RNA Biomedicine 2016-present Member, Cellular and Molecular Biology Program 2017-present University of Michigan, Ann Arbor, MI Postdoctoral Scholar, Genetics 2010-2014 Stanford University, Stanford, CA; Advisor: Dr. Michael Snyder Postdoctoral Associate, Computational Biology Spring 2010 Duke University, Durham, NC; Advisor: Dr. Terrence S. Furey

### Scholarships, Fellowships, and Honors

2017	NSF CAREER Award
2016	Institutional nominee for W.M. Keck Foundation Medical Science Research Program
2016	Institutional nominee for Searle Scholar Award
2015–2017	Alfred P. Sloan Foundation Fellowship in Computational & Evolutionary Molecular Biology
2013–2014	NIH Pathway to Independence Award (K99/R00) [1K99HG007356-01]
2012	AAAS/Science Program for Excellence in Science
2005–2008	NSF Graduate Research Fellowship
2005–2009	James B. Duke Fellowship
Summer 2004	Mayo Clinic Summer Undergraduate Research Fellow
2003	Barry M. Goldwater Memorial Scholarship
Summer 2003	The Institute for Genomic Research (TIGR) Summer Fellow
2001	Robert C. Byrd Honors Scholarship
2001	Mississippi State University Presidential Scholarship
2001	National Merit Scholarship

### **Grant Support**

#### Active

U41 HG009293 (Multi PI: Cherry, Boyle)
NIH/NHGRI Total Costs: \$2,171,753
RegulomeDB: A Resource for the Human Regulome
This project seeks to expand and support a RegulomeDB, a database for prioritizing and predicting functional variants in the human genome.

2017–2022 DBI-1651614 (PI: Boyle)

Total Costs: \$979,984 NSF/BIO/DBI

CAREER: Conservation of cohesin-containing cis regulatory modules in the human and mouse lineages

The goal of this project is the study of the turnover of cohesin binding sites in the human and mouse genomes.

2017-2018

Eleanor and Larry Jackier U-M/Technion and Weizmann Collaborative Research Grant

(PI: Boyle, Mandel-Gutfreund)

Michigan - Israel Partnership for Research & Education

Total Costs: \$50,000 Identifying novel disease related mutations in the genomic environments around Trascription Fac-

tor binding sites The goal of this project is to identify variants in the proximity of TF binding sites that have an indirect effect on their binding.

### Completed

R00 HG007356 Pathway to Independence Award (K99/R00) 2013-2017 (PI: Boyle)

Total Costs: \$987,771 NIH/NHGRI

Global Discovery and Validation of Functional Regulatory Elements

This project seeks to extend current assays demonstrating function of genomic regions into an equivalent genome-wide assay.

FG-2015-65465 2015-2017 (PI: Boyle)

Alfred P. Sloan Foundation Total Costs: \$50,000

Fellowship in Computational & Evolutionary Molecular Biology

2016-2020 R01 HL130705

(PI: Willer; Co-I with Effort) Total Costs: \$2,784,005 NIH/NHLBI

Large-scale human genetics to understand molecular mechanisms of atrial fibrillation and related

This project seeks to provide new insights into atrial fibrillation mechanisms through wholegenome screening.

### **Professional Service**

#### Service

DCM&B Preliminary Exam Abstract Review Committee (PARC) [Chair 2018–current] 2017-current

DHG Faculty Recruitment and Promotions Committee 2017-current

DCM&B Faculty Recruitment Committee 2016-current

DCM&B Seminar Series Committee [Chair 2016–current] 2016-current

DCM&B Admissions Committee 2015-current

**DHG Computational Support Committee** 2015-2017

DCM&B Retreat Planing Committee Chair (including 1st annual) 2015-2016 Ad hoc admissions reviewer, University of Michigan DCM&B 2014

Member, International Society for Computational Biology (ISCB) 2013-current

Member, American Association for the Advancement of Science (AAAS) 2012-current

Duke Computational Biology & Bioinformatics student committee 2008-2009

Member, Gamma Sigma Delta Agricultural Honor Society 2005-current

### **Reviewing Activity**

Ad hoc reviewer for the journals: Nature Genetics, Genome Research, Genome Biology, Nature Since 2009

Neuroscience, Nature Communications, Nature Protocols, Bioinformatics, Nucleic Acids Research, BMC Bioinformatics, Oncotarget, Scientific Reports, Atherosclerosis, BioEssays, Gene

Program Committee, Great Lakes Bioinformatics and Canadian Computational Biology Conference 2015-curent (GLBIO/CCBC)

Program Committee, Algorithms for Computational Biology (ALCOB) 2015-2016

Reviewer for UK Medical Research Council (RCUK MRC) 2015

Reviewer for UK Biotechnology and Biological Sciences Research Council (RCUK BBSRC) 2015

2015	Reviewer for Michigan Institute for Clinical & Health Research (MICHR) Postdoctoral Translational
	Scholars Program
2013-current	Program Committee, Gene Regulation and Transcriptomics, ISMB/ECCB
2012-2015	DNA Day Essay Contest Detailed Review Judge for ASHG
2012	Distinguished contributor as a leading reviewer for the journal Bioinformatics

# **Teaching and Mentorship**

# Teaching

2017	Panel member, U. Michigan "New Faculty Orientation to Corporate & Foundation Relations" [70]
	attendees]
2017	Experimental Genetics Systems (HUMGEN 632) [Course Director]
2016	Experimental Genetics Systems (HUMGEN 632) [1 discussion]
2015-current	Gene Structure and Regulation (HUMGEN 541) [3 lectures + 2 discussions / yr.]
2015-current	Introduction to Bioinformatics & Computational Biology (BIOINF 527) [2 lectures + 3 labs / yr.]
2015-current	Bioinformatics Journal Club (BIOINF 602/603)
2015-current	Basic Biology for Graduate Students with Quantitative Training (BIOINF 523) [2 lectures / yr.]
2014	Panel memnber, BIOINF 527 "Challenges in Biology, Biomedicine, Data & Analysis"
2010	Co-taught Cold Spring Harbor Systems Biology Pre-meeting Workshop
2009	Duke student panelist for "How to prepare for and get into graduate school"
2008	Taught Duke mini-course on Genome Browsers & Databases
Fall 2003	Lab TA for Isotopes Tech I (MS. State, BCH 4414)

# Mentorship

### **Graduate Students**

2017-current	Melissa Englund (Ph.D. Student, Human Genetics, University of Michigan)
	NIH Human Genetics Training Program (T32)
2017-current	Samuel Zhao (M.S. Student, Bioinformatics, University of Michigan)
2016-current	Haley Amemiya (Ph.D. Student, Cellular and Molecular Biology, University of Michigan)
	NIH Cellular & Molecular Biology Training Program (T32)
	Rackham Graduate Student Research Grant (pre-candidate)
2016-current	Shriya Sethuraman (Ph.D. Student, Bioinformatics, University of Michigan)
2016-current	Shengcheng Dong (Ph.D. Student, Bioinformatics, University of Michigan)
2016-current	Christopher Castro (Ph.D. Student, Bioinformatics, University of Michigan)
	NIH Bioinformatics Training Program (T32)
	Rackham Merit Fellow
	Rackham Graduate Student Research Grant (pre-candidate)
2015-current	Ningxin Ouyang (Ph.D. Student, Bioinformatics, University of Michigan)
2015-current	Torrin McDonald (Ph.D. Student, Human Genetics, University of Michigan)
	NIH Human Genetics Training Program (T32)
	Rackham Graduate Student Research Grant (pre-candidate)
2015–2017	Greg Farnum (Ph.D. Student, Cellular and Molecular Biology, University of Michigan)
2015-current	Sierra Nishizaki (Ph.D. Student, Human Genetics, University of Michigan)
	NIH Genome Science Training Program (T32)
	Rackham Merit Fellow
	Rackham Summer Award

# **Additional Graduate Rotation Students**

2017	Amanda Moccia (Rotation Student, Human Genetics, University of Michigan)
2017	Stephen Carney (Rotation Student, Human Genetics, University of Michigan)
2016	Tingyang Li (Rotation Student, Bioinformatics, University of Michigan)

## **Undergraduate and High School Students**

2016–2017	Cody Morterud (Undergraduate, UROP Computer Science, University of Michigan)
2016-2017	Colten Williams (Undergraduate, UROP Computer Science, University of Michigan)

2016–2017	Courtney Asman (Undergraduate, Neuroscience, University of Michigan)
2014–2017	Maxwell Spadafore (Undergraduate, LS&A Honors Informatics, University of Michigan)
2013-2014	Natalie Ng (High School, Stanford Institutes of Medicine Summer Research)
2013-2014	Dana Wyman (Undergraduate, Biology, Stanford University)
2013	Justin Young (High School, Stanford Institutes of Medicine Summer Research)
2012	Melanie Connick (Undergraduate, Biology, University of New Mexico)
2012	Edward Dai (Undergraduate, Computer Science, Stanford University)

#### **Doctoral Thesis Committees**

2018-current	Negar Farzaneh (Bioinformatics, University of Michigan)
2018-current	Rucheng Diao (Bioinformatics, University of Michigan)
2017-current	Steven Romanelli (Molecular & Integrative Physiology, University of Michigan)
2017-current	Amanda Moccia (Human Genetics, University of Michigan)
2017-current	Christopher Lee (Biostatistics, University of Michigan)
2016-current	Mohd Hafiz Bin Mohd Rothi (Molecular, Cellular, and Developmental Biology, University of Michi-
	gan)
2015-current	Ari Allyn-Feuer (Bioinformatics, University of Michigan)
2015-2017	Raymond Cavalcante (Bioinformatics, University of Michigan)
2015–2017	Zhengting Zou (Bioinformatics, University of Michigan)

### **Preliminary Exam Committees**

2018	Mitch Fernandez (Bioinformatics, University of Michigan)
2017	Tingyang Li (Bioinformatics, University of Michigan)
2017	Marcus Sherman (Bioinformatics, University of Michigan)
2017	Adrienne Shami (Human Genetics, University of Michigan)
2017	Trenton Frisbie (Human Genetics, University of Michigan)
2017	Melissa Englund (Human Genetics, University of Michigan)
2017	Peter Orchard (Bioinformatics, University of Michigan)
2017	Li Guan (Bioinformatics, University of Michigan)
2016	Shriya Sethuraman (Bioinformatics, University of Michigan)
2016	Jed Carlson (Bioinformatics, University of Michigan)

### **Industry Experience**

2013–2014 Consultant, Color Genomics
Personalized medicine / genomics startup

#### **Publications**

\* Indicates co-first authorship † Indicates co-senior authorship underscore indicates lab members

- [1] <u>Diehl AG</u>, **Boyle AP**. "Conserved and species-specific transcription factor co-binding patterns drive divergent gene regulation in human and mouse." *Nucleic Acids Research* 2018, :gky018.
- [2] Nielsen JB, Fritsche LG, Zhou W, Teslovich TM, Holmen OL, Gustafsson S, Gabrielsen ME, Schmidt EM, Beaumont R, Wolford BN, Lin M, Brummett CM, Preuss MH, Refsgaard L, Bottinger EP, Graham SE, Surakka I, Chu Y, Skogholt AH, Dalen H, **Boyle AP**, Oral H, Herron TJ, Kitzman J, Jalife J, Svendsen JH, Olesen MS, Njølstad I, Løchen ML, Baras A, Gottesman O, Marcketta A, O'Dushlaine C, Ritchie MD, Wilsgaard T, Loos RJF, Frayling TM, Boehnke M, Ingelsson E, Carey DJ, Dewey FE, Kang HM, Abecasis GR, Hveem K, Willer CJ. "Genomewide Study of Atrial Fibrillation Identifies Seven Risk Loci and Highlights Biological Pathways and Regulatory Elements Involved in Cardiac Development." *American Journal of Human Genetics* 2017. PMID: 29290336.
- [3] Spadafore M, Najarian K, Boyle AP. "A proximity-based graph clustering method for the identification and application of transcription factor clusters." *BMC Bioinformatics* 2017, 18:530. PMID: 29187152.
- [4] \*Yang B, \*Zhou W, \*Jiao J, Nielsen JB, Mathis MR, Heydarpour M, Lettre G, Folkersen L, Prakash S, Schurmann C, Fritsche L, <u>Farnum GA</u>, Lin M, Othman M, Hornsby W, Driscoll A, Levasseur A, Thomas M, Farhat L, Dubé MP, Isselbacher EM, Franco-Cereceda A, Guo Dc, Bottinger EP, Deeb GM, Booher A, Kheterpal S, Chen YE, Kang HM, Kitzman J, Cordell HJ, Keavney BD, Goodship JA, Ganesh SK, Abecasis G, Eagle KA, **Boyle AP**, Loos RJF,

- †Eriksson P, †Tardif JC, †Brummett CM, †Milewicz DM, †Body SC, †Willer CJ. "Protein-altering and regulatory genetic variants near GATA4 implicated in bicuspid aortic valve." *Nature communications* 2017, 8:15481. PMID: 28541271.
- [5] Nishizaki SS, Boyle AP. "Mining the Unknown: Assigning Function to Noncoding Single Nucleotide Polymorphisms." *Trends in Genetics* 2017, 33:34–45. PMID: 27939749.
- [6] Diehl AG, Boyle AP. "Deciphering ENCODE." Trends in Genetics 2016, 32(4):238-249. PMID: 26962025.
- [7] Phanstiel DH, **Boyle AP**, Heidari N, Snyder MP. "Mango: A bias correcting ChIA-PET analysis pipeline." *Bioinformatics* 2015. PMID: 26034063.
- [8] \*Cheng Y, \*Ma Z, Kim BH, Wu W, Cayting P, **Boyle AP**, Sundaram V, Xing X, Dogan N, Li J, Euskirchen G, Lin S, Lin Y, Visel A, Kawli T, Yang X, Patacsil D, Keller CA, Giardine B, Mouse ENCODE Consortium, Kundaje A, Wang T, Pennacchio LA, Weng Z, †Hardison RC, †Snyder MP. "Principles of regulatory information conservation between mouse and human." *Nature* 2014, 515(7527):371–375. PMID: 25409826.
- [9] \*Yue F, \*Cheng Y, \*Breschi A, \*Vierstra J, \*Wu W, \*Ryba T, \*Sandstrom R, \*Ma Z, \*Davis C, \*Pope BD, \*Shen Y, Pervouchine DD, Djebali S, Thurman RE, Kaul R, Rynes E, Kirilusha A, Marinov GK, Williams BA, Trout D, Amrhein H, Fisher-Aylor K, Antoshechkin I, DeSalvo G, See LH, Fastuca M, Drenkow J, Zaleski C, Dobin A, Prieto P, Lagarde J, Bussotti G, Tanzer A, Denas O, Li K, Bender MA, Zhang M, Byron R, Groudine MT, McCleary D, Pham L, Ye Z, Kuan S, Edsall L, Wu YC, Rasmussen MD, Bansal MS, Kellis M, Keller CA, Morrissey CS, Mishra T, Jain D, Dogan N, Harris RS, Cayting P, Kawli T, Boyle AP, Euskirchen G, Kundaje A, Lin S, Lin Y, Jansen C, Malladi VS, Cline MS, Erickson DT, Kirkup VM, Learned K, Sloan CA, Rosenbloom KR, Lacerda de Sousa B, Beal K, Pignatelli M, Flicek P, Lian J, Kahveci T, Lee D, Kent WJ, Ramalho Santos M, Herrero J, Notredame C, Johnson A, Vong S, Lee K, Bates D, Neri F, Diegel M, Canfield T, Sabo PJ, Wilken MS, Reh TA, Giste E, Shafer A, Kutyavin T, Haugen E, Dunn D, Reynolds AP, Neph S, Humbert R, Hansen RS, De Bruijn M, Selleri L, Rudensky A, Josefowicz S, Samstein R, Eichler EE, Orkin SH, Levasseur D, Papayannopoulou T, Chang KH, Skoultchi A, Gosh S, Disteche C, Treuting P, Wang Y, Weiss MJ, Blobel GA, Cao X, Zhong S, Wang T, Good PJ, Lowdon RF, Adams LB, Zhou XQ, Pazin MJ, Feingold EA, Wold B, Taylor J, Mortazavi A, Weissman SM, Stamatoyannopoulos JA, Snyder MP, Guigo R, Gingeras TR, Gilbert DM, Hardison RC, Beer MA, Ren B, Mouse ENCODE Consortium. "A comparative encyclopedia of DNA elements in the mouse genome." Nature 2014, 515(7527):355-364. PMID: 25409824.
- [10] \*Boyle AP, \*Araya CL, Brdlik C, Cayting P, Cheng C, Cheng Y, Gardner K, Hillier LW, Janette J, Jiang L, Kasper D, Kawli T, Kheradpour P, Kundaje A, Li JJ, Ma L, Niu W, Rehm EJ, Rozowsky J, Slattery M, Spokony R, Terrell R, Vafeados D, Wang D, Weisdepp P, Wu YC, Xie D, Yan KK, Feingold EA, Good PJ, Pazin MJ, Huang H, Bickel PJ, Brenner SE, Reinke V, Waterston RH, Gerstein M, †White KP, †Kellis M, †Snyder M. "Comparative analysis of regulatory information and circuits across distant species." *Nature* 2014, 512(7515):453–456. PMID: 25164757.
- [11] Araya CL, Kawli T, Kundaje A, Jiang L, Wu B, Vafeados D, Terrell R, Weissdepp P, Gevirtzman L, Mace D, Niu W, **Boyle AP**, Xie D, Ma L, Murray JI, Reinke V, Waterston RH, Snyder M. "Regulatory analysis of the C. elegans genome with spatiotemporal resolution." *Nature* 2014, 512(7515):400–405. PMID: 25164749.
- [12] Phanstiel DH, **Boyle AP**, Araya CL, Snyder MP. "Sushi.R: flexible, quantitative and integrative genomic visualizations for publication-quality multi-panel figures." *Bioinformatics* 2014. PMID: 24903420.
- [13] \*Xie D, \*Boyle AP, \*Wu L, Kawli T, Zhai J, Snyder M. "Dynamic trans-acting factor colocalization in human cells." *Cell* 2013, 155(3):713–724. PMID: 24243024.
- [14] \*Kasowski M, \*Kyriazopoulou-Panagiotopoulou S, \*Grubert F, \*Zaugg JB, \*Kundaje A, Liu Y, **Boyle AP**, Zhang QC, Zakharia F, Spacek DV, Li J, Xie D, Steinmetz LM, Hogenesch JB, Kellis M, Batzoglou S, Snyder M. "Extensive variation in chromatin states across humans." *Science* 2013, 342(6159):750–752. PMID: 24136358.
- [15] **Boyle AP**, Hong EL, Hariharan M, Cheng Y, Schaub MA, Kasowski M, Karczewski KJ, Park J, Hitz BC, Weng S, Cherry JM, Snyder M. "Annotation of functional variation in personal genomes using RegulomeDB." *Genome Research* 2012, 22(9):1790–1797. PMID: 22955989.
- [16] Schaub MA, **Boyle AP**, Kundaje A, †Batzoglou S, †Snyder M. "Linking disease associations with regulatory information in the human genome." *Genome Research* 2012, 22(9):1748–1759. PMID: 22955986.

- [17] The ENCODE Project Consortium. "An integrated encyclopedia of DNA elements in the human genome." *Nature* 2012, 489(7414):57–74. PMID: 22955616.
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- [19] \*Chen R, \*Mias GI, \*Li-Pook-Than J, \*Jiang L, Lam HYK, Chen R, Miriami E, Karczewski KJ, Hariharan M, Dewey FE, Cheng Y, Clark MJ, Im H, Habegger L, Balasubramanian S, O'Huallachain M, Dudley JT, Hillenmeyer S, Haraksingh R, Sharon D, Euskirchen G, Lacroute P, Bettinger K, Boyle AP, Kasowski M, Grubert F, Seki S, Garcia M, Whirl-Carrillo M, Gallardo M, Blasco MA, Greenberg PL, Snyder P, Klein TE, Altman RB, Butte AJ, Ashley EA, Gerstein M, Nadeau KC, Tang H, Snyder M. "Personal omics profiling reveals dynamic molecular and medical phenotypes." Cell 2012, 148(6):1293–1307. PMID: 22424236.
- [20] \*Song L, \*Zhang Z, \*Grasfeder LL, \*Boyle AP, \*Giresi PG, \*Lee B, \*Sheffield NC, Graff S, Huss M, Keefe D, Liu Z, London D, McDaniell RM, Shibata Y, Showers KA, Simon JM, Vales T, Wang T, Winter D, Zhang Z, Clarke ND, †Birney E, †Iyer VR, †Crawford GE, †Lieb JD, †Furey TS. "Open chromatin defined by DNaseI and FAIRE identifies regulatory elements that shape cell-type identity." *Genome Research* 2011, 21(10):1757–1767. PMID: 21750106.
- [21] The ENCODE Project Consortium. "A user's guide to the encyclopedia of DNA elements (ENCODE)." *PLoS Biology* 2011, 9(4):e1001046. PMID: 21526222.
- [22] **Boyle AP**, Song L, Lee B, London D, Keefe D, Birney E, Iyer VR, †Crawford GE, †Furey TS. "High-resolution genome-wide in vivo footprinting of diverse transcription factors in human cells." *Genome Research* 2011, 21:456–464. PMID: 21106903.
- [23] \*Stitzel ML, \*Sethupathy P, Pearson DS, Chines PS, Song L, Erdos MR, Welch R, Parker SCJ, **Boyle AP**, Scott LJ, Margulies EH, Boehnke M, Furey TS, Crawford GE, Collins FS. "Global epigenomic analysis of primary human pancreatic islets provides insights into type 2 diabetes susceptibility loci." *Cell Metabolism* 2010, 12(5):443–455. PMID: 21035756.
- [24] McDaniell R, Lee B, Song L, Liu Z, **Boyle AP**, Erdos MR, Scott LJ, Morken MA, Kucera KS, Battenhouse A, Keefe D, Collins FS, Willard HF, Lieb JD, Furey TS, †Crawford GE, †Iyer VR, †Birney E. "Heritable individual-specific and allele-specific chromatin signatures in humans." *Science* 2010, 328(5975):235–239. PMID: 20299549.
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- [26] Babbitt CC, Fedrigo O, Pfefferle AD, **Boyle AP**, Horvath JE, Furey TS, Wray GA. "Both noncoding and protein-coding RNAs contribute to gene expression evolution in the primate brain." *Genome Biology and Evolution* 2010, 2:67–79. PMID: 20333225.
- [27] Xu X, Tsumagari K, Sowden J, Tawil R, **Boyle AP**, Song L, Furey TS, Crawford GE, Ehrlich M. "DNaseI hypersensitivity at gene-poor, FSH dystrophy-linked 4q35.2." *Nucleic Acids Research* 2009, 37(22):7381–7393. PMID: 19820107.
- [28] **Boyle AP**, Furey TS. "High-resolution mapping studies of chromatin and gene regulatory elements." *Epigenomics* 2009, 1(2):319–329. PMID: 20514362.
- [29] **Boyle AP**, Guinney J, Crawford GE, Furey TS. "F-Seq: a feature density estimator for high-throughput sequence tags." *Bioinformatics* 2008, 24(21):2537–2538. PMID: 18784119.
- [30] **Boyle AP**, Davis S, Shulha HP, Meltzer P, Margulies EH, Weng Z, †Furey TS, †Crawford GE. "High-resolution mapping and characterization of open chromatin across the genome." *Cell* 2008, 132(2):311–322. PMID: 18243105.

- [31] **Boyle AP**, Boyle JA. "Global analysis of microbial translation initiation regions." In *Journal of the Mississippi Academy of Sciences*, *Volume 48* 2003:138–150.
- [32] **Boyle AP**, Boyle JA. "Visualization of aligned genomic open reading frame data." *Biochemistry and Molecular Biology Education* 2003, 31:64–68.
- [33] Wan X, Boyle JA, Bridges SM, **Boyle AP**. "Interactive clustering for exploration of genomic data." In *Proceedings* of the Artificial Neural Networks in Engineering Conference, Volume 12, St. Louis, MO 2002:753–758.

### **Patents**

[34] Karczewski K, Snyder M, Butte AJ, Dudley JT, Hong E, Boyle A, Cherry MJ. "Method and system for the use of biomarkers for regulatory dysfunction in disease." 2013, (US Patent Application 20130116931).