Dr James Kennedy

Director of neuroscience research program, 500 ‘articles’

Main research interest is susceptibility genes for psychiatric disorders

Found lots of marker genes for psych. disorders

1. Current Status of Schizophrenia genetic studies
   1. 108 genetic loci associated with sch. – 2014 paper
      1. Very very large paper (424 authors)
      2. Huge effort
      3. Genome wide study using 37,000
      4. MHC, DRD2 genes
      5. Strongest association (lowest p-value) is MHC on chromosome 6 – bigger than all other significant sites
      6. Odds ratio 1.05, 1.06 is typical (5% risk increase, accounts for fractions of these variants)
   2. Genome-wide association studies suggest limited gene enrichment in sch. Compared to 5 autoimmune diseases
      1. Pull out snps that were functionally related to the immune system – 700 or so
      2. These did not predict risk for sch.
      3. There were 6 immune genes that were associated, but they all also have roles in brain development
   3. Complement c4 gene is located in the MHC region peak
      1. Haplotype enigma?
      2. John Nash – Kennedy ate dinner with him – cool
      3. Complement component 4
      4. This c4 gene is nestled inside all the high-complexity HLA genes
      5. HLA are antibod genes?
      6. Endovirus? Same as retrovirus? Intron exon
      7. Complement binds to neurons and synapses
      8. Long vs. short – retroviral insertion determines this
      9. Utah is a standard European genetic group
      10. AL-AL on the same chromosome is the high risk group (11% of Caucasians)
      11. Enigma of the haplotypes!
          1. Solved by McCarroll
          2. Can’t just do a single PCR and measure, since all the repeats, pseudogenes and hyper-variability of the region obscure the genetic signal
          3. We can’t do PCR on all these people anyway – ethics concern
          4. Need to do it with only chip data (few hundred SNPs)
          5. Measure a few SNPs on either side to figure out what variant exists
      12. Droplet Digital PCR
          1. Do the same pcr 20,000 times and look at the distribution
          2. Solve the problem!
      13. The more copies of C4A, the more expression
      14. The more copies of C4-HERV, the more copys of A vs. B
      15. Low correlation vs. c4 and nearby SNPs
      16. Look up Jennie Pouget