

Topics in Neurobiology and Behavior: Focus on Autism-related Research GU4440

Fall 2020, Thursdays 4.10-6PM

Schermerhorn 405

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Office hours: Friday 3-5pm, Schermerhorn 356 (watch out for the correct 356, not with booths)

Course overview: Research on autism spectrum disorder, or ASD, is highly multi-disciplinary, because it is a behaviorally defined disorder known to depend strongly on genetics. We will explore the nature of ASD by examining studies in genetics, epidemiology, neurobiology and behavior. We will examine the results from neurobiological experiments on animal models of ASD at the behavioral, systems, cellular, molecular and genetic levels. Questions to be considered will include: Is ASD really a single disorder? Which theories of ASD causation are the most compelling? Has there really been a rise in ASD prevalence? What makes a good animal model of ASD? Can neurobiological experiments on animals lead to treatments for ASD? Can any oddities of animal behaviors be considered directly analogous to those comprising a human behavioral disorder? Will the future bring "personalized medicine" with dedicated animal or human stem cell models for every person with ASD? What types of environmental insult contribute to ASD? What are the links between the immune and nervous systems in ASD? How do current behavioral findings from people with ASD direct neurobiological research?

Prerequisites: Mind, Brain and Behavior (Psych 1010) or an equivalent biological-based psychology class is required. Courses in statistics, research methods or genetics would be helpful, but are not required. The permission of the instructor is required in order to register.

Course objectives: This course fulfills the Seminar Requirement for the Psychology Major and the Advanced Seminar Requirement for the Neurobiology and Behavior Major.

The goals of this course are:

- to gain an advanced understanding of neurobiological and other research related to ASD by reading primary scientific literature
- to read, understand and orally present primary scientific literature from psychology and neuroscience journals
- to critically evaluate published research and discuss its merits, caveats and alternative interpretations
- to develop a review commentary or research proposal on a research topic by reading and evaluating published research

#### **Course requirements:**

**Weekly readings/assignment and participation (20%):** Everyone is expected to carefully and thoroughly read and understand two scientific research papers each week. The chosen papers will usually be primary research reports from seminal findings on the topic of the week. In some cases, supplemental reviews will also be posted and are optional but will usually be very helpful. Everyone will post a comment, thought or question on each of the two readings, before class on the Discussion Board of CourseWorks, which will serve as a basis for discussion during class (at least a longish paragraph on each). Each week, Dr. Brew will usually also present relevant background material relevant for the upcoming week.

**Presentation of two papers (40%):** Each week, 2 student leaders will each present one of the assigned readings in an approximately **30 minute slide presentation and initiate a short class discussion**. Each student will present 2 or more papers during the semester. Although all students are expected to have tried to understand the readings, and posted on them, the presenter should try to add a little more breadth and depth, and propose two or three questions for the class discussion. Guidelines on how to give a good presentation will be posted on CourseWorks. Feedback will be provided one week following the presentation. Obtain help with your presentation by meeting with Dr. Brew well before class, e.g. during Friday office hours. (These meetings are always agreed to be exceedingly useful, especially because of the sophistication and multi-disciplinary nature of the research studies. Dr. Brew will usually be able to agree other meeting times, as needed). Note that on the week when you are presenting, you need

**Short mid-term (5%):** (This is very casual and easy to do well on, so don't worry!) All students take a half-hour long **written midterm quiz** covering the material presented in class by Dr. Brew and the students. 8 minutes will be short questions, and 15 minutes will be longer written answers taking 5 minutes and 10 minutes on topics you can choose from among many options. This will take place on Thursday 22<sup>nd</sup> October, and will be with open notes. The main reason for having it is to give Dr. Brew an idea of your writing skills and where your strengths lie for the factual material, which will help in choosing the most appropriate term project topic.

**Term paper (either a research review or a research proposal) (30%):** A **term paper** will be required, on a topic of your choosing from material covered during the seminar (~10-15pg, 3,000-5,000 words). Detailed information will be given at the start of the course and detailed guidelines will also be posted. You are required to get Dr. Brew's approval on your choice of topic. Short outline due October 29<sup>th</sup>. (REALLY IMPORTANT to submit this promptly). A draft of your term paper should be submitted by December 3<sup>rd</sup> and the final version on December 10<sup>th</sup>. However, note that if you submit your draft earlier than December 3<sup>rd</sup>, the more help you will receive in honing your draft to perfection.....that help usually results in at least one or two shifts up the grade scale.

**Short presentation based on term paper (5%):** Each student will give a **ten minute presentation** of an interesting aspect of their term project paper on December 10<sup>th</sup>, the final day of class. Two prizes of autism-related books will be provided by Dr. Brew for the "audience favorite" presentations (everyone gets two votes, and the two presentations with the most votes win.....topmost gets first choice of book).

#### **Class policies:**

**Attendance:** You are expected to come to class each week prepared to discuss the assigned papers. Your unexcused absence will be noted and reflected in your participation grade. Make-up 'participation' for preapproved excused absences will be arranged on an individual basis.

**Assignments:** Paper presentations are assigned based on solicited preferences during the first week of the semester and once assigned can be changed only with Dr. Brew's approval. In the case of a documented medical or family emergency, alternate arrangements will be made to present the paper on another week or if necessary privately during office hours. Please bear in mind that schedule changes can be very inconvenient for Dr. Brew and the rest of the class, so give as much of a heads-up as you can if you need to reschedule.

**Academic Integrity:** "The intellectual venture in which we are all engaged requires of faculty and students alike the highest level of personal and academic integrity. As members of an academic community, each one of us bears the responsibility to participate in scholarly discourse and research in a manner characterized by intellectual honesty and scholarly integrity. . . . In practical terms, this means that, as students, you must be responsible for the full citations of others' ideas in all of your research papers and projects; you must be scrupulously honest when taking your examinations; you must always submit your own work and not that of another student, scholar, or internet agent." From the Faculty Statement on Academic Integrity - [www.college.columbia.edu/academics/integrity-statement](http://www.college.columbia.edu/academics/integrity-statement). Cheating on assignments or exams and plagiarism are very serious violations within the academic community. Students are expected to do their own work on all tests and assignments for this class. You are expected to always act in accordance with the Columbia honor code. Any student found cheating or plagiarizing in this class will be reported to Columbia's Office of Judicial Affairs and Community Standards for evaluation and academic discipline. If you have questions about any aspect of academic integrity at Columbia, please refer to the following link: [www.college.columbia.edu/academics/integrity](http://www.college.columbia.edu/academics/integrity) and if you have specific questions about the judicial process, please see [www.college.columbia.edu/academics/disciplinaryprocess](http://www.college.columbia.edu/academics/disciplinaryprocess).

#### Class Schedule

Please note that readings and topics may be subject to change based on enrollment number and student preferences. Papers in bold numbered 1 and 2, are the recommendations for student presentations, and for your posts. (In some cases two or three short papers are grouped and count as one presentation, but you can choose to read and post on only one of the group, if you are not the presenter). The remaining (unbolded) papers are optional background reading.....read at any depth you like.....either skim-read to get overview and perspective, or delve further if it suits your particular areas of expertise. The exception to this usual pattern is in weeks 4 and 5, when it is fine to choose an unbolded paper to present, or to post on. (This is because there are so many good animal model papers that Dr. Brew cannot find it in her heart to leave any out of play).

#### Week 1. September 10th. What is ASD? Plus introduction to seminar format

Information on: course format, evaluation, discussion board posts, presentation of papers, class discussion, term paper. **Students will select at least one of their presentation topics today.** Please choose one paper from weeks 2-7, the other from weeks 8-12. (If there is time Dr. Brew will sometimes include brief presentations of any uncovered papers).

#### Introduction to ASD and theories of autism

The clinical definition and diagnosis of ASD, including broadening definition and changes in diagnostic criteria over time. The strong genetic basis of autism, concordance. Theories: Excitatory-inhibitory imbalance, theory of mind, neural disconnection, overgrowth,

male brain, noisy brain, synaptic dysfunction, faulty synaptic pruning, striatum/cerebellum/frontal cortex, environmental effects, (vaccines).

1. **REVIEW: Rubenstein, J. L. R., & Merzenich, M. M. (2003). Model of autism: increased ratio of excitation/inhibition in key neural systems. *Genes, brain, and behavior*, 2(5), 255–67.**

This paper introduced one of the well-known theories of autism: excitatory/inhibitory imbalance. The fact that epilepsy is a common co-morbidity with ASD means this was not all that controversial, in broad terms. However, note that E/I imbalance in ASD must be thought of with nuance, because a large majority of epileptics do not have ASD.

2. **REVIEW: Sztainberg Y, and Zoghbi HY (2016) Lessons learned from studying syndromic autism spectrum disorders. *Nat Neurosci*. Oct 26;19(11):1408-1417.**

Ben-Shalom R1, Keeshen CM2, Berrios KN3, An JY4, Sanders SJ4, Bender KJ5 (2017) Opposing Effects on Nav1.2 Function Underlie Differences Between SCN2A Variants Observed in Individuals With Autism Spectrum Disorder or Infantile Seizures. *Biol Psychiatry*. Aug 1;82(3):224-232. This is quite neuro heavy.

### Week 2. September 17th. Examples of behavioral and neurobiological abnormalities in ASD.

Biological motion perception, abnormal cerebrospinal fluid volume, empathy versus social cognition, noisy brain, language. Baby sib studies/biomarkers.

1. **Klin, A., Lin, D., Gorrindo, P., Ramsey G., & Jones, W. (2009) Two-year-olds with autism orient to non-social contingencies rather than biological motion. *Nature*, 459(7868), 257-263.** (Note this is quite easy and fun to present, so a good choice if your neuro is limited).

2. **Shen MD, Kim SH, McKinstry RC, Gu H, Hazlett HC, Nordahl CW, Emerson RW, Shaw D, Elison JT, Swanson MR, Fonov VS, Gerig G, Dager SR, Botteron KN, Paterson S, Schultz RT, Evans AC, Estes AM, Zwaigenbaum L, Styner MA, Amaral DG, Piven J; Infant Brain Imaging Study Network; Infant Brain Imaging Study Network (2017) Increased Extra-axial Cerebrospinal Fluid in High-Risk Infants Who Later Develop Autism. *Biol Psychiatry*. Aug 1;82(3):186-193.**

PSYCH: Swanson MR1, Shen MD1, Wolff JJ2, Boyd B1, Clements M3, Rehg J3, Elison JT2, Paterson S4,5, Parish-Morris J5, Chappell JC1, Hazlett HC1, Emerson RW1, Botteron K6, Pandey J5, Schultz RT5, Dager SR7, Zwaigenbaum L8, Estes AM7, Piven J1; IBIS Network (2017) Naturalistic Language Recordings Reveal "Hypervocal" Infants at High Familial Risk for Autism. *Child Dev*. 2017 Mar 10.

PSYCH fMRI: Bird G, Silani G, Brindley R, White S, Frith U, Singer T. (2010) Empathic brain responses in insula are modulated by levels of alexithymia but not autism. *Brain*. 2010 May;133(Pt 5):1515-25.

NEURO fMRI: Dinstein, I., Heeger, D. J., Lorenzi, L., Minshew, N. J., Malach, R., & Behrmann, M. (2012). Unreliable evoked responses in autism. *Neuron*, 75(6), 981–91. An example of a neurobiologically measured difference between male adolescents with autism and controls.

NEURO fMRI: Hahamy, A., Behrmann, M., & Malach, R. (2015). The idiosyncratic brain: distortion of spontaneous connectivity patterns in autism spectrum disorder. *Nature Neuroscience*, 18(2), 302–9.

### Week 3. September 24th. The genetics of ASD. Chromosomal deletions and duplications conferring risk. Syndromic autism versus "idiopathic" autism. Specific genes conferring risk. Abnormal expression of networks of synaptic genes and microglia genes.

1. **Willsey et al., (2013) Co-expression networks implicate human midfetal deep cortical projection neurons in the pathogenesis of autism. *Cell*, 155(5): 997–1007.**

2. Voineagu, I., Wang, X., Johnston, P., Lowe, J. K., Tian, Y., Horvath, S., Mill, J., et al. (2011). Transcriptomic analysis of autistic brain reveals convergent molecular pathology. *Nature*, **474**(7351), 380–4.

REVIEW: Chang, J., Gilman, S. R., Chiang, A. H., Sanders, S. J., & Vitkup, D. (2014). Genotype to phenotype relationships in autism spectrum disorders. *Nature Neuroscience*, *18*(2), 191–8.

Sanders SJ, He X, Willsey AJ, Ercan-Sencicek AG, Samocha KE, Cicek AE, Murtha MT, Bal VH, Bishop SL, Dong S, Goldberg AP, Jinlu C, Keaney JF 3rd, Klei L, Mandell JD, Moreno-De-Luca D, Poultney CS, Robinson EB, Smith L, Solli-Nowlan T, Su MY, Teran NA, Walker MF, Werling DM, Beaudet AL, Cantor RM, Fombonne E, Geschwind DH, Grice DE, Lord C, Lowe JK, Mane SM, Martin DM, Morrow EM, Talkowski ME, Sutcliffe JS, Walsh CA, Yu TW; Autism Sequencing Consortium (2015) Insights into Autism Spectrum Disorder Genomic Architecture and Biology from 71 Risk Loci. *Neuron*. Sep 23;87(6):1215-1233.

Bernier R. et al (2014) Disruptive *CHD8* Mutations Define a Subtype of Autism Early in Development. *Cell* Volume 158, Issue 2, p263–276, 17 July 2014

Kong SW, Sahin M, Collins CD, Wertz MH, Campbell MG, Leech JD, Krueger D, Bear MF, Kunkel LM, Kohane IS (2014) Divergent dysregulation of gene expression in murine models of fragile X syndrome and tuberous sclerosis. *Mol Autism*. 2014 Feb 24;5(1):16.

Gaugler et al. (2014) Most genetic risk for autism resides with common variation. *Nature Genetics*, Aug;46(8):881-5. And a Sandin et al “do-over”, correcting the calculated percentage risk.

Weeks 4 and 5. October 1<sup>st</sup> and 8<sup>th</sup>. What makes a good animal model? Is it possible to model ASD? Specific syndromes associated with ASD and specific genes

Face validity, construct validity and predictive validity as applied to animal models of ASD. Which (if any) animal behaviors are analogous to human ASD behavioral symptoms? Repetitive behaviors and social abnormalities. Consideration of developmental age, and species and strain differences. Advances due to CRISPR techniques. Mouse models of synaptic-associated genes implicated in ASD: Fragile X syndrome, Dravet syndrome, Timothy syndrome, *SCN1A* and *SHANK* genes. ASD-related genes that seem less directly related to synapses: Rett syndrome, *CHD8*, *PTEN*, *Ube3a*

For these two weeks the four student presenters may pick whichever papers they like the look of, based on their interest in a particular syndrome and/or gene (my four favorites are in bold):

Henderson, C., Wijetunge, L., Kinoshita, M. N., Shumway, M., Hammond, R. S., Postma, F. R., Brynczka, C., et al. (2012). Reversal of disease-related pathologies in the fragile X mouse model by selective activation of GABA<sub>B</sub> receptors with arbaclofen. *Science translational medicine*, *4*(152), 152ra128.

**Han, S., Tai, C., Westenbroek, R. E., Yu, F. H., Cheah, C. S., Potter, G. B., Rubenstein, J. L., et al. (2012). Autistic-like behaviour in *Scn1a*<sup>+/-</sup> mice and rescue by enhanced GABA-mediated neurotransmission. *Nature*, **489**(7416), 385–90.**

Selimbeyoglu A, Kim CK, Inoue M, Lee SY, Hong ASO, Kauvar I, Ramakrishnan C, Fenno LE, Davidson TJ, Wright M, Deisseroth K. (2017) Modulation of prefrontal cortex excitation/inhibition balance rescues social behavior in CNTNAP2-deficient mice. *Sci Transl Med*. 2017 Aug 2;9(401).

**Peça, J., Feliciano, C., Ting, J. T., Wang, W., Wells, M. F., Venkatraman, T. N., Lascola, C. D., et al. (2011). *Shank3* mutant mice display autistic-like behaviours and striatal dysfunction. *Nature*, **472**(7344), 437–42.**

Chao, H.-T., Chen, H., Samaco, R. C., Xue, M., Chahrour, M., Yoo, J., Neul, J. L., et al. (2010). Dysfunction in GABA signalling mediates autism-like stereotypies and Rett syndrome phenotypes. *Nature*, *468*(7321), 263–9.

Huang, H.-S., Allen, J. A., Mabb, A. M., King, I. F., Miriyala, J., Taylor-Blake, B., Sciaky, N., et al. (2012). Topoisomerase inhibitors unsilence the dormant allele of *Ube3a* in neurons. *Nature*, 481(7380), 185–9.

Xiong, Q., Oviedo, H. V, Trotman, L. C., & Zador, A. M. (2012). *PTEN* regulation of local and long-range connections in mouse auditory cortex. *The Journal of neuroscience*, 32(5), 1643–52.

**NEW!** Zhou Y, Sharma J, Ke Q, Landman R, Yuan J, Chen H, Hayden DS, Fisher JW 3rd, Jiang M, Menegas W, Aida T, Yan T, Zou Y, Xu D, Parmar S, Hyman JB, Fanucci-Kiss A, Meisner O, Wang D, Huang Y, Li Y, Bai Y, Ji W, Lai X, Li W, Huang L, Lu Z, Wang L, Anteraper SA, Sur M, Zhou H, Xiang AP, Desimone R, Feng G, Yang S. (2019) Atypical behaviour and connectivity in SHANK3-mutant macaques. *Nature*. Jun;570(7761):326-331.

Orefice LL, Mosko JR, Morency DT, Wells MF, Tasnim A, Mozeika SM, Ye M, Chirila AM, Emanuel AJ, Rankin G, Fame RM, Lehtinen MK, Feng G, Ginty DD. (2019) Targeting Peripheral Somatosensory Neurons to Improve Tactile-Related Phenotypes in ASD Models. *Cell*. 2019 Aug 8;178(4):867-886.e24. This paper is super-interesting and is a follow-up to a 2016 paper from the same lab.

Krey, J. F., Paşca, S. P., Shcheglovitov, A., Yazawa, M., Schwemberger, R., Rasmusson, R., & Dolmetsch, R. E. (2013) Timothy syndrome is associated with activity-dependent dendritic retraction in rodent and human neurons. *Nature neuroscience*, 16(2), 201–9. (This is also suited to the topic of week 12, “cells in dishes”).

#### Week 6. October 15<sup>th</sup> Characteristics of autism in females

The two behavioral papers go together, and count as one in terms of posting or presenting.

1. Jacquemont S. et al. *Am. J. Hum. Genet.* 94, 415-425 (2014) A higher mutational burden in females supports a "female protective model" in neurodevelopmental disorders.
- 2a. Frazier T.W. et al. *J. Am. Acad. Child Adolesc. Psychiatry*53, 329-340 (2014) Behavioral and cognitive characteristics of females and males with autism in the Simons Simplex Collection.
- 2b. Head A.M. et al. *Mol. Autism* 5, 19 (2014) Gender differences in emotionality and sociability in children with autism spectrum disorders.

Week 7. October 22<sup>nd</sup>. Short mid-term quiz for first half hour of class (see Course Requirements section above for more details).

Do particular parts of the brain show structural or functional abnormalities in ASD? Where in the brain should we look, based on behavioral evidence from people with ASD? Social brain areas? Movement areas? Which parts of the brain are abnormal in ASD or mouse models of ASD? (E.g. striatum, forebrain, cerebellum).

1. Stoner, R., Chow, M. L., Boyle, M. P., Sunkin, S. M., Mouton, P. R., Roy, S., Wynshaw-Boris, A., et al. (2014). Patches of disorganization in the neocortex of children with autism. *The New England journal of medicine*, 370(13), 1209–19.

#### 2. TBD

Ellegood, J., Anagnostou, E., Babineau, B. A., Crawley, J. N., Lin, L., Genestine, M., DiCicco-Bloom, E., et al. (2015). Clustering autism: using neuroanatomical differences in 26 mouse models to gain insight into the heterogeneity. *Molecular psychiatry*, 20(1), 118–25.

#### Week 8. October 29th. The vaccine story. ALSO TERM PAPER OULINE DUE DATE.

There is a huge amount of literature on this whole story, which is more sociology (scare journalism, mass hysteria, conspiracy theories) than psychology, let alone neuroscience. Most importantly please read and post on one or both of the epidemiology studies (papers 1a and 1b).

1a. Jain A, Marshall J, Buikema A, Bancroft T, Kelly JP, Newschaffer CJ. (2015) Autism occurrence by MMR vaccine status among US children with older siblings with and without autism. *JAMA*, Apr 21;313(15):1534-40.

1b. Smeeth L, Cook C, Fombonne E, Heavey L, Rodrigues LC, Smith PG, Hall AJ (2004) MMR vaccination and pervasive developmental disorders: a case-control study. *Lancet*, Sep 11-17;364(9438):963-9.

## 2. The retracted Wakefield et al paper and commentaries since:

**The RETRACTED** paper: Wakefield AJ, Murch SH, Anthony A, Linnell J, Casson DM, Malik M, Berelowitz M, Dhillon AP, Thomson MA, Harvey P, Valentine A, Davies SE, Walker-Smith JA (1998). Ileal-lymphoid-nodular hyperplasia, non-specific colitis, and pervasive developmental disorder in children. *Lancet*. Feb 28;351(9103):637-41

**The RETRACTION:** Eggertson, L, (2010) Lancet retracts 12-year-old article linking autism to MMR vaccines. *CMAJ*, Mar 9;182(4):E199-200.

And here is a link to a series of papers by the main journalist uncovering what went wrong.....

<http://briandeer.com/solved/bmj-secrets-series.htm>

## Week 9. November 5th. Biomarkers and early diagnosis, further baby sib studies

1. Elsabbagh, M., Mercure, E., Hudry, K., Chandler, S., Pasco, G., Charman, T., Pickles, A., et al. (2012). Infant neural sensitivity to dynamic eye gaze is associated with later emerging autism. *Current biology : CB*, 22(4), 338–42. A possible biomarker for early screening.
2. Emerson RW, Adams C, Nishino T, Hazlett HC, Wolff JJ, Zwaigenbaum L, Constantino JN, Shen MD, Swanson MR, Elison JT, Kandala S, Estes AM, Botteron KN, Collins L, Dager SR, Evans AC, Gerig G, Gu H, McKinsty RC, Paterson S, Schultz RT, Styner M; IBIS Network, Schlaggar BL, Pruett JR Jr, Piven J. (2017) Functional neuroimaging of high-risk 6-month-old infants predicts a diagnosis of autism at 24 months of age. *Science Translational Medicine*. Jun 7;9(393).

## Week 10. November 12<sup>th</sup>. Maternal infection.....immune system and gut....probiotics

(also relevant to microglia, synaptic pruning, mTOR)

1. Lee et al (2015) Maternal hospitalization with infection during pregnancy and risk of autism spectrum disorders. *Brain Behav Immun*. Feb;44:100-5.....this is a study of 2.4 million people showing risk of autism increases by 37% if Mom hospitalized with infection.
2. Maternal gut bacteria promote neurodevelopmental abnormalities in mouse offspring. Kim S, Kim H, Yim YS, Ha S, Atarashi K, Tan TG, Longman RS, Honda K, Littman DR, Choi GB, Huh JR (2017) *Nature*. Sep 28;549(7673):528-532. (Plus companion paper Yim et al and prior study Choi et al).

(Hsiao et al (2013) Microbiota modulate behavioral and physiological abnormalities associated with neurodevelopmental disorders. *Cell*. 2013 Dec 19;155(7):1451-63). This paper helps to explain the background of the three papers for topic two.

## Week 11. November 19th. Treatment approaches from classroom to clinic

For this week, each presenter will pick a pair of papers from the pairings below and present them together.....they are short. Post on two pairs of papers.

### 1. TWO PAPERS ON CLASSROOM TREATMENTS

1a. Shire SY, Chang YC, Shih W1, Bracaglia S, Kodjoe M, Kasari C (2017) Hybrid implementation model of community-partnered early intervention for toddlers with autism: a randomized trial. *J Child Psychol Psychiatry*. May;58(5):612-622.

1b. Kasari C, Rotheram-Fuller E, Locke J, Gulsrud A. (2012) Making the connection: randomized controlled trial of social skills at school for children with autism spectrum disorders. *J Child Psychol Psychiatry*. 2012 Apr;53(4):431-9.

2. TWO PAPERS ON PMD Bozdagi, O., Tavassoli, T., & Buxbaum, J. D. (2013). Insulin-like growth factor-1 rescues synaptic and motor deficits in a mouse model of autism and developmental delay. *Molecular autism*, 4(1), 9.

Kolevzon, A., Bush, L., Wang, A. T., Halpern, D., Frank, Y., Grodberg, D., Rapaport, R., et al. (2014). A pilot controlled trial of insulin-like growth factor-1 in children with Phelan-McDermid syndrome. *Molecular autism*, 5(1), 54

3. TWO PAPERS ON FRAGILE X

Gantois I, Khoutorsky A, Popic J, et al (2017) Metformin ameliorates core deficits in a mouse model of fragile X syndrome. *Nat Med*. 2017 Jun;23(6):674-677.

Berry-Kravis et al (2012) Effects of STX209 (arbaclofen) on neurobehavioral function in children and adults with fragile X syndrome: a randomized, controlled, phase 2 trial. *Sci Transl Med*. 2012 Sep 19;4(152).

November 26<sup>th</sup> is Thanksgiving, a university holiday.

Week 12. December 3<sup>rd</sup>. Can cells in dishes help find ASD treatments?

1. Mariani J, Coppola G, Zhang P, Abyzov A, Provini L, Tomasini L, Amenduni M, Szekely A, Palejev D, Wilson M, Gerstein M, Grigorenko EL, Chawarska K, Pelphrey KA, Howe JR, Vaccarino FM (2015). FOXP1-Dependent Dysregulation of GABA/Glutamate Neuron Differentiation in Autism Spectrum Disorders. *Cell*, Jul 16;162(2):375-90.

2. Shcheglovitov, A., Shcheglovitova, O., Yazawa, M., Portmann, T., Shu, R., Sebastiano, V., Krawisz, A., et al. (2013). SHANK3 and IGF1 restore synaptic deficits in neurons from 22q13 deletion syndrome patients. *Nature*, 503(7475), 267–71.

Week 13. December 10<sup>th</sup>. Which theories of ASD are the most compelling? Which research should be most urgently funded?

Presentations of Term Papers: Persuade the class of your opinion or convince the class that we should fund your research proposal (10 minutes each). No assigned reading this week.