05/12/2014 Tel conversation with Tom Otis

Tom Dan and Stefan

BAC paper

Mutant atxn2 changes translation in hek cells, replicated in the BAC model.

Can put together with the story of mechanistic function of atxn2, associates with lot of rna binding proteins.

Enhanced degradation or by delaying translation.

Interacts w staufen 1 with a role in mRNA decay

Tom asks about splicing, but we have not found anyting to show atxn2 acts in splicing, and we have not found that atxn2 binds a2bp1 either.

RGS8, do we need functional data on loss of Rgs8? RGS6 seems to be decreased, and Rgs6 leads to ataxia. Rgs4 down but not as significant.

Tom asks maybe there are some G protein biochemical assays.

Tom can look at g-protein signaling in the cerebellar slice

ASOs are working… most effective relative late. 13 weeks.

Tom could look at firing, DHPG induced firing, 2-3 animals can get a result.

With 2 photon calcium imaging they are doing, are costly.

Consider sending Tom 3 saline mice and 3 ASO mice, pcp2-tg mice.

Tom says at 24 weeks there is a big effect.

Ask Isis to do a second round of more modified ASOs.

And we can do transcriptome

Also started to make a 3rd animal model, with endogenous promoter on cDNA.

Meera – will have mice breeding in about 3 months,

They will provide us tail or piece of the slice for genotyping.

Will ask Pattie right now to send Tom 3 animals each of saline and ASO treated. We will pick ones that perform well on ASO and poorly on saline.

Ilya should send us some ASOs for ITPR1

--doesn’t see how serious the reviews are.

Atxion compounds in the grant? Now they say that they have oral compounds, so that would aid in the problem that our compounds are difficult to deliver. –target the slow ca regulated calcium channels.

PPG grant, will need to resubmit in February, because won’t have the BAC paper published.

Need to evaluate the olive in the brain stem, in the BAC mice.

Synaptic calcium annotation

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