

**Agenda**  
**Hirschsprung Disease Research Collaborative (HDRC) Conference Call**  
**December 7<sup>th</sup>, 3:00pm EST**

Attendees (Aravinda Chakravarti and Courtney Berrios, Johns Hopkins University; Michael Rollins, University of Utah; Dorothy Rocourt, Penn State Hershey Medical Center; Lisa Iamcelli, UCLA; Jana Creps; University of Michigan; Kara Kronemeyer, Phoenix Children's Hospital; Ankush Gosain, University of Tennessee Health Science Center; JoAnn DeRosa, All Children's Hospital; Phil Frykman, Cedars-Sinai Medical Center; Douglas Tamura, Valley Children's Hospital; Representative (missed name), Cincinnati Children's)

- I. Welcome – Aravinda Chakravarti welcomed everyone to the call and thanked them for joining the call and their continued work with the HDRC.
- II. HDRC Update (see attached HDRC Membership table)
  - a. Membership – Courtney Berrios reported that we've had no new IRB approvals in the last quarter, but the University of Tennessee Health Science Center has submitted their IRB application and it is in review.
  - b. Samples – Ms. Berrios also reported that enrollments over the last quarter have slowed down a bit. Texas Children's enrolled 1 new family, Cincinnati Children's 3 families, Children's Healthcare of Atlanta 2 families, Nationwide Children's 1 family, University of Utah 1 family with full samples and data plus 7 families with data awaiting sample collection, and Seattle Children's 5 families. This brings our total enrollment for the HDRC to 291 affected individuals and 391 of their unaffected family members.
- III. Grant resubmission
  - a. Review – Dr. Chakravarti and Phil Frykman reported that we have received the reviews back from our re-submission of the HDRC grant in the July 2015 cycle. It received an impact score of 41; which is in the 23<sup>rd</sup> percentile. This is better than the previous review but not good enough to be funded. The NIDDK program officer was enthusiastic about the grant, but it again went to a study section that did not have the relevant expertise. The revised grant received similar criticisms to the initial submission including:
    - i. Even if we identify factors that put an individual at high risk for specific complications, how would that change their clinical management?
    - ii. Making correlations between risk factors and outcomes is innovative, but finding new genes is not that innovative.
    - iii. They did not believe we had provided enough evidence that we could enroll the needed numbers of participants and collect complete data.
    - iv. We need to include a biostatistician.
    - v. The hypotheses proposed are non-specific.
  - b. Next Steps – The Program Steering Committee (PSC) has met to discuss the review and discussed a plan for the steps below.

- i. Revise and re-submit for a future cycle doing a better job of addressing the criticisms and providing specific examples of how clinical management could be impacted by the work.
- ii. Consider submission of parts of this proposal and the HDRC 's work to other funding agencies such as PCORI and the Robert Wood Johnson Foundation Pioneer Award.
- iii. Complete some analyses on the samples and data we have on the existing 290 cases to show the richness of the data and possibilities of findings. Dr. Chakravarti is beginning to analyze some targeted variants in these samples.
- iv. In order to get feedback from the membership, the PSC will abstract some of the comments from the review and share with HDRC members. We welcome feedback from all HDRC members.

Q. Michael Rollins asked if we had exome sequence data on all HDRC participants that could be analyzed. Dr. Chakravarti responded that we do not have funds for exome sequencing now, but can do some targeted markers.

Q. Dr. Rollins also asked if the reviewers appear to want a more focused grant. Drs. Chakravarti and Fryman responded that they didn't think they specifically wanted a more focused grant, but did want more specific ideas of how patient management would be impacted. They felt that surgery was an effective treatment and were not convinced that the study would improve upon this. We need to make a better case of this.

Q. Ankush Gosain asked if the review gave impression that they are interested in funding questions that the HDRC could address, but not the structure of data and sample collection. Drs. Chakravarti and Frykman responded that the reviewers named one of the strengths of the proposal to be the national collaborative and biorepository, so they seem to be supportive of this if they better liked the questions asked of the repository data and samples.

- IV. Advisory Board – Dr. Chakravarti reported that the PSC has moved forward on building an HDRC Advisory Board that can provide independent input on HDRC activities. He was happy to say that Belinda Dickie at Cincinnati Children's has agreed to chair the Advisory Board. Dr. Dickie is now working with the PSC to determine the rest of the Board, taking into account suggestions the PSC received in the past. If anyone has suggestions of members for the advisory board or wishes to nominate themselves, please contact Aravinda Chakravarti, Courtney Berrios or Dr. Dickie.

Thank you to everyone for joining the call!