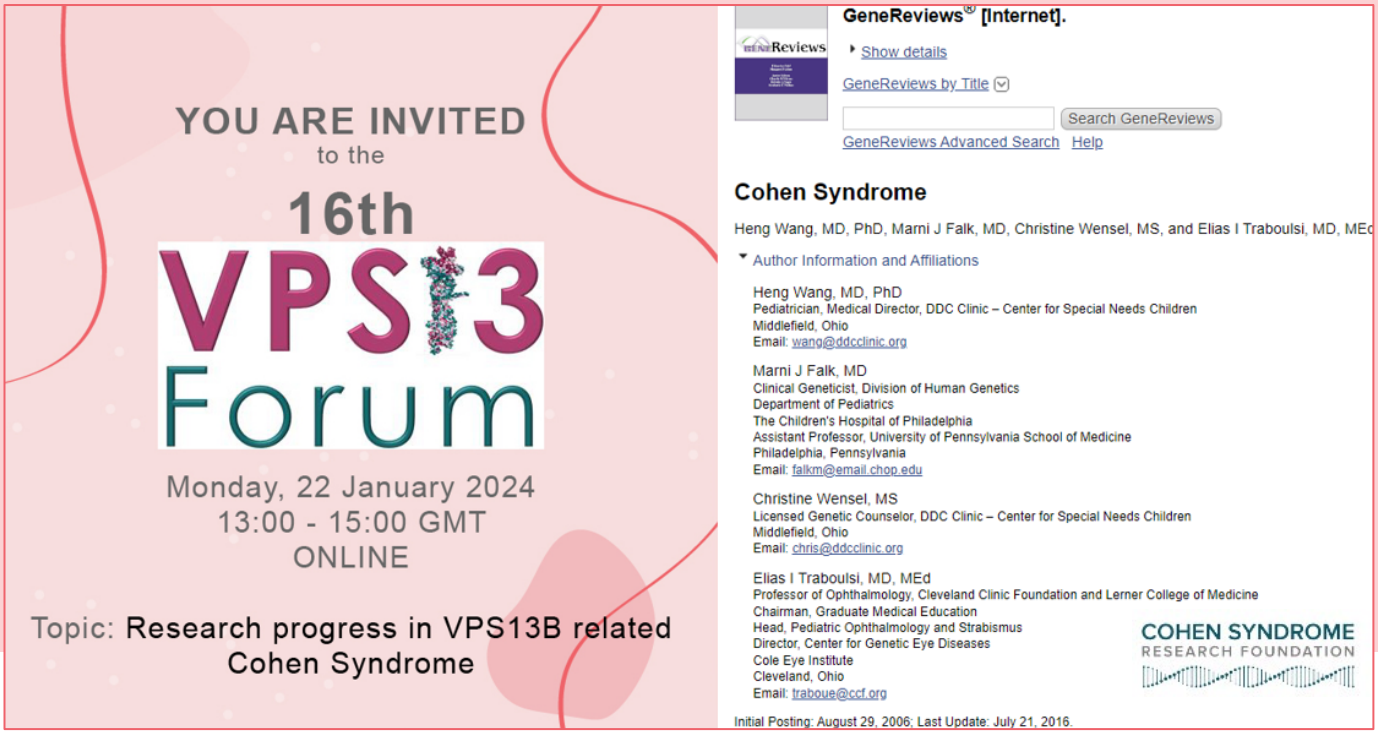

MEETING REPORT
January 2024

Thank you

To the organisers and hosts:

Dr. Muhammad Ansar
Dr. Kevin Peikert

To all our speakers and especially to everyone in the Cohen Syndrome communities who joined us!

To all attendees and everyone reading this report and helping spreading the word.

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INTRODUCTION

The large, evolutionarily conserved VPS13 (vacuolar protein sorting 13) proteins are newly identified lipid transport proteins that localise to membrane contact sites (MCSs), regions where organelle membranes are tethered in close apposition. Mutations in the genes encoding the 4 homologous VPS13 proteins are associated with distinct neurological disorders: chorea-acanthocytosis - *VPS13A*, Cohen Syndrome - *VPS13B*, one type of early onset Parkinson's disease - *VPS13C* and one type of ataxia - *VPS13D*.

The Cohen Syndrome (CS) clinical manifestations are:

- failure to thrive in infancy and truncal obesity starting in the teen years
- early-onset hypotonia (weak muscle tone) and developmental delays
- affectionate behaviours, cheerful disposition
- microcephaly (small head circumference) developing during first year of life
- moderate to profound psychomotor disability
- characteristic facial features
- night blindness and myopia (near-sightedness)
- retinal dystrophy (causing progressive vision loss)
- neutropenia (low white blood cells contributing to frequent illness and infection).

Dr Muhammad Ansar, University of Lausanne, Switzerland kindly organised the content of the forum and co-hosted it with Dr Kevin Peikert, University of Rostock, Germany.

PRESENTATIONS

1.
Cohen Syndrome: What does the diagnosis mean for families

Ashley Waterman, Cohen Syndrome Research Foundation joined from Los Angeles at the very early local hours and it was inspiring to hear how the Foundation works tirelessly to improve the lives of the Cohen Syndrome children and their families by supporting and advancing research.

There are 1,000 individuals diagnosed worldwide and the community covers 30 countries. The Foundation provides information resources for the families and they are a repository for medical professionals looking for standards of care and research studies.

In partnership with UCLA's Autism Intervention Research network on Physical Health (AIR-P) they brought together a group of nationwide Cohen Syndrome experts which is working on publishing a paper that will be a resource for parents and physicians around the world.

2.
Clinical spectrum of Cohen Syndrome – 20 years of continued discovery

Dr Heng Wang, Medical Director, DDC Clinic for Special Needs Children, Middlefield, OH, USA took us through decades from when the syndrome was identified, through the progress of the research projects. Dr Wang followed an unusual career path which enabled him to do meaningful work and this is highlighted in the article published in the career section of *Science* Journals.

The clinic has patients from Ohio plus 30 other states in the USA, as well as from Canada, Australia, New Zealand, and from across Europe and Asia.

3.
Drug screening for Cohen Syndrome (CS) - from cells to mice
Dr Fabrizio Vacca, Jules Gonin Eye Hospital, University of Lausanne, Switzerland spoke about the main goal of Dr Ansar's research group of developing therapeutic strategies. The models used are *VPS13B* cell lines and a CS mouse model.

Their approaches explore three main areas:

- investigation of the pathological mechanisms of CS
- gene therapy options
- phenotypic drug screening.

4.
Modelling of Cohen Syndrome with brain organoid technology
Professor Woong Sun and Professor Jungmin Choi, Department of Biomedical Sciences, Korea University, Seoul, Korea.

Brain organoids are an exciting new technology with the potential to significantly change our understanding of the development of the human brain and of its disorders. With step-by-step differentiation protocols, three-dimensional neural tissues are self-organised from pluripotent stem cells and recapitulate the major milestones of human brain development *in vitro*. Studies have shown that brain organoids can mimic the spatiotemporal dynamics of neurogenesis, the formation of regional neural circuitry, and the integration of glial cells into a neural network. This suggests that brain organoids could serve as a representative model system to study the human brain.

5.
New insights into the neurobiology of *VPS13B* in Cohen Syndrome
Dr Binnaz Yalcin, Centre for Translational and Molecular medicine, Dijon, France spoke about the neurobiology of *VPS13B* as studied in mouse models:

- the *VPS13B*-mutant mice displayed parallel clinical manifestations to those seen in CS patients
- identified previously unreported neuropathological findings
- uncovered neurodegeneration as the main cause of the microcephaly phenotype in mice and likely mechanisms in humans
- both sexes shared features, with some phenotypes being less pronounced or absent in females, both in mice and in patients.

CONCLUSION

While the clinical manifestations are rather different from VPS13A and XK diseases, there are some interesting observations in the way the research progressed throughout the past couple of decades and there is room for collaboration between the NA and CS scientific communities.

Subsequently the plans for the next NA Symposium in 2025 is to be held together with the CS community. It's likely that it will be somewhere on the West coast of the United States, where there are some relevant projects going on.

Along with the scientific aspects there are also possible collaboration opportunities between the charitable organisations to promote and increase their visibility and their awareness work and this may result in widening the funding opportunities.

Our Trustee, Professor Dr Adrian Danek highlighted that interestingly, the research presented in the last talk in particular shows increasing similarity with respect to neurodegeneration and is a natural common focus.

NEXT VPS13 FORUM

17th Forum - Monday, 29 April 2024, 13:00 – 15:00 GMT (find your local time)
The exact timings and agenda will be confirmed through the zoom invitation from Dr Kevin Peikert.

Thank you!

ADVOCACY FOR NEUROACANTHOCYTOSIS PATIENTS

NA ADVOCACY USA
NEUROACANTHOCYTOSIS ADVOCACY USA, INC.

info@naadvocacy.org

www.naadvocacy.org

www.naadvocacyusa.org