国際視覚聴覚二重障害医療シンポジウム 2026 年 2 月 20 日（金）　講演抄録

Abstract 1 17：35 ～ 18：05

Usher syndrome: the underlying genetic defects and their identification

Usher 症候群：遺伝的原因とその同定

座長：岩田 岳（東京医療センター 臨床研究センター 分子細胞生物学研究　名誉部長）

Speaker: Prof. Hannie Kremer
Dept Otorhinolaryngology and Dept Human Genetics, Radboudumc, Nijmegen, The Netherlands

Abstract:

Usher syndrome is characterized by recessive inheritance of sensorineural hearing loss and retinal degeneration of the type called retinitis pigmentosa. Also vestibular dysfunction can be associated with the syndrome. Four clinical types of Usher syndrome (I-IV) are distinguished which is based on the age of onset and progression of hearing loss and the presence or absence of symptoms of vestibular dysfunction. Also, cases have been described with atypical Usher syndrome. Genetic subtyping of the four clinical types is based on the genes that harbour the causative defects. So far, ten genes have been associated with the syndrome and several of these are among the largest genes in the human genome.

A genetic diagnosis is important for patients and their families in order to receive optimal genetic counselling and information on prognosis as well as for the patient's eligibility for (future) clinical trials and therapies. The fast developments in DNA sequencing allowed the improvement of medical genetic testing which developed from single gene testing to gene panel sequencing or exome sequencing and further to genome sequencing. Currently, state-of-the-art medical genetic testing results in a genetic diagnosis in the majority of cases with Usher syndrome. However, as for other rare diseases, there are cases that remain genetically 'unsolved'. Two important reasons for that are limitations of detection and of interpretation of DNA variants. These will be discussed in the presentation.

Another important point that will be addressed is that a number of genes associated with Usher syndrome is also associated with nonsyndromic hearing loss. As hearing loss associated with these genes is congenital both in case of Usher syndrome and nonsyndromic hearing loss, medical genetic testing is often performed in early childhood. This can lead to uncertainty of the prognosis with regard to retinal degeneration as this occurs later in childhood or in adolescence.

Ongoing and future developments in detection of DNA variants and, importantly, in their interpretation are expected to further improve medical genetic testing in Usher syndrome as well as other rare disorders.

Abstract 2 18：05 ～ 18：35

Medical Care and Clinical Research for Deafblindness in Otolaryngology

耳鼻咽喉科における視覚聴覚二重障害の医療と臨床研究

座長：神崎 晶（東京医療センター 臨床研究センター 聴覚・平衡覚研究部 聴覚障害研究室 室長）

Speaker: Prof. Ronald Pennings

Dept Otorhinolaryngology, Radboud University Medical Center, Nijmegen, The Netherlands

Abstract:

In this presentation an overview will be presented on the clinical care provided to subjects born with a sensorineural hearing loss who undergo genome sequencing to identify the cause of hearing loss. A substantial part of these subjects will be identified with a genetic form of deafblindness and Usher syndrome is the most prominent and important genetic diagnosis that can be encountered. The following questions will be addressed in this presentation:

- How do you counsel parents and subjects on genome sequencing for congenital sensorineural hearing loss?
- How do we counsel parents and subjects in whom we have identified pathogenic variants in one of the Usher syndrome genes?
- How do you inform parents about the uncertainties of future visual function in subjects with genetic defects in Usher syndrome type 1 genes?
- How do you discuss finding pathogenic variants in Usher type 2 genes?

Counseling of parents of these subjects is complex and emotional. Guidance in this process and future perspectives that can be used for counseling are presented based on clinical research of Usher syndrome. In addition, the progress in the development of genetic therapies is emphasized.

Abstract 3 18：40 ～ 19：10

Clinical management and research for deaf-blindness in Ophthalmology

眼科における視覚聴覚二重障害の医療と研究

座長：岩田 岳（東京医療センター 臨床研究センター 分子細胞生物学研究　名誉部長）

Speaker: Prof. Mariya Moosajee
Moorfields Eye Hospital and UCL Institute of Ophthalmology, London, The United Kingdom

Abstract:

There are several causes of deaf-blindness, the most common worldwide is Usher sydrome. Some rarer conditions can be misdiagnosed as Usher syndrome, such as PHARC syndrome. In this talk, I will go through the clinical management that we offer patients presenting with dual sensory hearing and sight loss, and emphasise the need for molecular diagnosis through genetic testing. I will share examples of some of the research we are undertaking to develop novel treatments for deafblind patients including non-viral gene therapy that can accomodate large genes such as USH2A, which is not amenable to conventional AAV vectors.

Abstract 4 19：10 ～ 19：40

Developing splicing modulation therapies for Usher syndrome type 2a: opportunities and challenges

Usher 症候群 2A 型に対するスプライシング調節療法の開発：可能性と課題

座長：神崎 晶（東京医療センター 臨床研究センター 聴覚・平衡覚研究部 聴覚障害研究室 室長）

Speaker: Prof. Erwin van Wijk
Dept Otorhinolaryngology, Radboud university medical center, Nijmegen, The Netherlands

Abstract:

Mutations in *USH2A* are the most frequent cause of both syndromic and non-syndromic retinitis pigmentosa (RP), for which currently no treatment options exist. It is generally believed that RP due to mutations in this gene is caused by a loss-of-function mechanism. In total, over 1500 different mutations have been identified in *USH2A* of which several are seen more frequently: c.2299delG (p.Glu767fs*21), c.2276G>T (p.Cys759Phe), c.7595-2144A>G (p.Lys2532Thrfs*56) and .

The size of the coding sequence (15,606 bp) and the presence of multiple alternatively spliced *USH2A* transcripts with unknown significance, hamper the development of gene augmentation therapy. Another difficulty in the development of a therapy is the lack of a suitable animal model. The currently available *Ush2a* mouse model displays only mild retina degeneration with a very late age of onset. Zebrafish *ush2a* mutant models however, show an early onset retinal dysfunction and are as such provide a unique opportunity to evaluate future therapeutic strategies.

Antisense oligonucleotide (ASO)-based splice modulation has been proven to hold great promise as a therapeutic strategy for a number of hereditary conditions, including Usher syndrome. Upon pre-mRNA binding, ASOs will prevent or stimulate binding of the spliceosome thereby modulating splicing events. ASOs can be designed and applied for different genes and genetic disorders as the specificity depends on their nucleotide sequence.

In this presentation opportunities and challenges in the (pre)clinical development of splicing modulation therapies for the future treatment of *USH2A*-associated retinal degeneration will be discussed.