RETINA INTERNATIONAL

Seeking A Cure For
Retinitis Pigmentosa, Macular Degeneration,
Usher Syndrome and Allied Retinal Dystrophies

RI USH SIG – Special Interest Group for Usher Syndrome at Retina International: Update on events & resource file on USH subtypes, genetic testing & USH genes

RI USH SIG
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We are happy to issue our Winter Newsletter providing you with an update of the latest and upcoming news relevant for people living with Usher Syndrome and with a resource file on USH subtypes, genetic testing and USH genes.

Save the date USH related events 2020

June 4-6. Reykjavík, Iceland.
RIWC 2020 - 21st Retina International World Congress
Retina International World Congress brings together some of the world's foremost retinal scientists and clinicians along with the global leaders in patient advocacy and peer support. The Nordic Ophthalmology Congress 2020 will take place at the same venue and time as RIWC 2020. During the events we are planning to hold an Usher Syndrome satellite meeting, details to be announced soon. www.riwc2020.is

June 26-27. Paris, France. 2020 International Usher info Symposium
Scientific & Patient Sympsoium organised by Fondation Pour l'Audition and Fondation Voir et Entendre in the framework of the LIGHT4DEAF project dedicated to Usher syndrome. http://pro.usherinfo.fr/2020-international-usher-info-scientific-symposium/

July 10-11. Austin. TX, United States
USH Connections Conference - Usher Syndrome Coalition
Learn the latest on developing treatments from leading US researchers and connect with impacted individuals, their families, and professionals serving the deafblind community.
https://www.usher-syndrome.org/our-story/ush-connections-conference-summaries.html

Recaps Autumn 2019

Inaugural Meeting of Retina International Special Interest Group on Usher Syndrome in Paris, 21 September 2019, Global Usher Awareness Day

At the occasion of Global Usher Syndrome Awareness Day on Saturday 21 September, the USH SIG Committee came together for a meeting in the Fondation de l'Audition in Paris. Dominique Sturz (Austria), Carol Brill (Ireland) and Dario Sorgato (Italy) enjoyed the warm welcome from hosts Marie-Josée Duran and Salma Hazgui of the Institut de l'Audition. Our fourth Committee member Melissa Chaikof (USA) joined the meeting by teleconference, thanks to the fantastic facilities at the venue. We were also pleased to welcome Professor Isabelle Audo of the Institut de la Vision, and Alice Lapujade (France).

The group discussed at great length the structure and strategy of USH SIG and we are happy to outline the following:

1. Proclamation: "We are a patient led group working together towards the provision of up to date relevant information about research and about expert research centers for people living with Usher Syndrome and advocating about the development of therapies for the global Usher Syndrome community."

2. Establishment of a Scientific Advisory Panel to ensure that information shared by USH SIG on scientific research on Usher Syndrome is accurate

3. Calendar of Events – to keep the Usher community informed of relevant events

4. Communication Strategy – information will be shared in a Newsletter format with national organisations associated with Usher Syndrome

ERN Eye Workshop on Clinical Trials & Research, 21-22 Nov 2019, Strasbourg

The workshop of the European Reference Network for Rare Eye diseases was preceded by the 2nd Sensgènes Annual Day, where the French affiliated center for Rare Sensory Diseases gave an update on the state-of-the-art research (ear and eye) done in France and with international collaboration.

At the ERN Eye workshop member states presented their updates on clinical trials of gene therapies and about access to and reimbursement of Luxturna (the first approved gene therapy for a rare eye disease: LCA due to REP65 mutation). Also treatment options under development in collaboration with international partners were discussed. For information on how to access genetic testing and clinical trials see our resource file about USH subtypes, USH genes and genetic testing below. For more info about clinical trials and full members and affiliated partners of ERN Eye see https://www.ern-eye.eu/map-of-the-centers-and-clinical-trials. An update about new full members will be available in 2020.

Resource file on USH subtypes, genetic testing & USH genes

USH 1 < 40%	USH 2 < 60%	USH 3 < 3%
Congenital deafness	Moderate to severe hearing loss	Mild hearing loss, progressing slowly
Night blindness in early childhood, first decade	Night blindness from teenage years	Night blindness from teenage years
Loss of peripheral vision and visuals acuity in first life decade	Loss of peripheral vision and visual acuity from teenage years	Slow progression of vision loss, later faster progression
1b about 25% of all Ushers	2a most common, about 50% of all Ushers	Very rare
1b, 1c, 1d, ..., 1k	2a, 2b, 2c, 2d	3a, 3b (new 2016)

Why is **genetic testing** important? Today, many promising treatments for Usher Syndrome in the lab and even in clinical trial are gene-based. Unless you know your subtype and even your mutation, you cannot know if you are **eligible for a clinical trial.** There are different types of potential gene therapies. Those that entail replacing the entire affected gene are not dependent on mutation, but some, such as gene editing or drugs that target specific mutations, require knowing not just the gene but also the mutation. In any case a genetically confirmed diagnosis is required to be eligible for clinical trials and also for upcoming treatments that are not mutation-specific. This is also for the patients' safety, because interventions and treatments can be harmful in cases of **differential diagnosis with similar phenotypes** (same symptoms).

In the EU most countries' health plans cover genetic testing if you are referred by your ENT specialist or ophthalmologist or retinal specialist to an expert center providing genetic testing. In some EU countries a hearing disorder diagnosed at newborn hearing screening is an indication for referral to genetic testing (Usher genes included). ERN Eye works on a common registry for Rare Eye Diseases, where member institutions will feed anonymized data with the patient's consent.
In the US, some insurance companies cover genetic testing. If an insurance company does not, Foundation Fighting Blindness, in partnership with Blueprint Genetics and InformedDNA®, offers an open access, no-cost genetic testing program called the My Retina Tracker Program® starting October 21st for individuals living in the United States, with a clinical diagnosis of an inherited retinal degeneration (IRD). For eligibility criteria see https://blueprintgenetics.com/my-retina-tracker-program/

USH Genes

USH Type	Locus	Gene	cDNA	Protein
USH1B	11q13.5	MYO7A	6.6 kb	Myosin VIIa
USH1C	11p14-15	USH1C	2.6 kb; isoforms	Harmonin
USH1D	11q21-q22	CDH23	10.8 kb; isoforms	Cadherin 23
USH1E	21q21	--		--
USH1F	10q11.2-q21	PCDH15	9 kb; isoforms	Protocadherin 15
USH1G	17q24-25	SANS	1.3 kb; isoforms	SANS
USH1H	15q22-23	--		--
(USH1J)	15q23-q25.1	CIB2	561 bp; isoforms	CIB2 now recognised to be mutated in isolated deafness
USH2A	1q41	USH2A	15.6 kb; isoforms	USH2A (Usherin)
USH2C	5q13	GPR98	18.9 kb; isoforms	GPR98 (VLGR1b)
USH2D	9q32-q34	DFNB31	4 kb; isoforms	Whirlin
USH3A	3q25	CLRN1	699 bp; isoforms	Clarin-1
USH3B		HARS		Histidyl-tRNA Synthetase
atypical USH	20q32.3	CEP250	7.3 kb; isoforms	Cep250
atypical USH	2p23.2	C2orf71	3.9 kb	C2orf71

Amendment from 26 Nov 2019 to our Autumn Newsletter on USH gene therapy: **USH2C:** A clinical trial based on mini-gene therapy and co-funded by CUREUsher (UK, IRL) and Stichting Ushersyndroom (NL) will be run at the Radboud University Medical Center (NL), more USH subtypes to come soon.

You can download our Autumn Newsletter on gene therapy for Usher Syndrome here: http://www.retina-international.org/ri-ush-newsletter-pdf/

We are very committed to making our communications accessible. If you wish to receive this newsletter in an alternative format, please let us know by emailing usher@retina-international.org and we will endeavour to issue future newsletters in your preferred format.

We hope you enjoyed our newsletter and resource file. We will come back to you with interesting news very soon and wish you a wonderful Christmas time and a Happy New Year!

To make sure not to miss out any important news about USH events, resource files, as well as research, clinical trials and surveys subscribe here: http://www.retina-international.org/updates-from-the-ri-ush-special-interest-group/

This Newsletter has been written by Dominique Sturz (AT), Melissa Chaikof (USA), Carol Brill (IRL) and Dario Sorgato (IT) and checked for accuracy and reliability by Pr. Isabelle Audo (FR).