



OPEN MEDICAL INSTITUTE

SEMINAR REPORT

NEUROLOGICAL AND SENSORY DISORDERS: GENES, PATHOGENESIS AND INNOVATIVE THERAPIES

March 13-19, 2022

A Global Educational Initiative by the
American Austrian Foundation

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SALZBURG INSTITUT PASTEUR SEMINAR IN NEUROLOGICAL AND SENSORY DISORDERS: GENES, PATHOGENESIS AND INNOVATIVE THERAPIES

March 13-19, 2022

31 fellows from 25 different countries
9 faculty members from France
16 lectures given by faculty
4 interesting round tables

Group Photo of Faculty and Fellows



**Salzburg Institut Pasteur Seminar in
Global Health: Neurological and Sensory Disorders: Genes, Pathogenesis and Innovative Therapies
Sunday, March 13 – Saturday, March 19, 2022**

		Sunday 13.03.2022	Monday 14.03.2022	Tuesday 15.03.2022	Wednesday 16.03.2022	Thursday 17.03.2022	Friday 18.03.2022	Saturday 19.03.2022
07:00	08:00		BREAKFAST	BREAKFAST	BREAKFAST	BREAKFAST	BREAKFAST	DEPARTURES
08:00	09:30		<u>08:15 - 09:15</u> Presentation Pasteur & Hearing Institutes	Brain Stimulation to Repair Deafness and Dyslexia Sophie Bouton	Blindness (Animal- and Cell-Based Modelling and Pathogenesis) Deniz Dalkara	Hearing Loss and Central Auditory Deficits: Emotion and Cognition S��verine Samson	Imaging the Human Eye: Tracking Anomalies in Defective and Aged Retinas Kate Grieve	
09:30	10:45		<u>09:15 - 10:15</u> Introductions <u>10:15 - 10:45</u> Pre-Seminar Test	Vision in Health (How the Eye Works?) Isabelle Audo	Hearing Loss (Animal- and Cell-Based Modelling and Pathogenesis) Aziz El-Amraoui	Treatment Solutions for Hearing Loss Saaid Safieddine	Treatment Solutions for Vision Loss Deniz Dalkara	
10:45	11:15		COFFEE BREAK	COFFEE BREAK	COFFEE BREAK	COFFEE BREAK	COFFEE BREAK	
11:15	12:30		Audition and Balance in Health (How the Inner Ear Works?) Evolution Matters Aziz El-Amraoui	Blindness (Isolated and Syndromic? Prevalence, Clinical Features, Causes, Diagnosis) Isabelle Audo	Hearing and Balance Deficits: From Animal Models to Humans Paul Avan	Impact of Ageing and External Factors: Hearing Paul Avan	Gene Therapy for Sensory Disorders: From Bench to Bedside Aziz El-Amraoui Deniz Dalkara	
12:30	14:00		LUNCH	LUNCH	LUNCH	LUNCH	LUNCH	
14:00	14:15		Case/ Key Questions Discussion	Case/ Key Questions Discussion	Free Afternoon	Case/ Key Questions Discussion	Case/ Key Questions Discussion	
14:15	15:15		Brain Computer Interface to Recover Movement and Communication Sophie Bouton	Deafness (Isolated & Syndromic? Prevalence, Clinical Features, Causes, Diagnosis) Sandrine Marlin		Music Interventions for Neurological Disorders S��verine Samson	Round Table Sense and Brain Therapies, Today and Tomorrow? (e.g. Advantages and Limitations of "Organ on Chip" Preclinical Modeling?) All Faculty	
15:15	16:15		Round Table Open Source (Tools and Softwares, Apps, ...) and Neuro-Sensory Precision Medicine All Faculty	Round Table Diagnoses of Cognitive and Sensory Rare Diseases and Genetic Counselling All Faculty		Round Table Brain, Senses, Environment and Healthy Aging? All Faculty		
16:15	17:00						Post-Seminar Test Evaluation & Discussion	
17:00	18:00		<u>17:00 - 17:15</u> OMI Presentation					
18:00	19:00	FACULTY MEETING TO REVIEW THE WEEK					FAREWELL RECEPTION	
19:00	20:00	WELCOME RECEPTION & DINNER	DINNER	DINNER	DINNER	DINNER	GRADUATION DINNER Certificates Awarded	
20:00	21:00					<u>20:30 - 21:30</u> CHAMBER MUSIC CONCERT		



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FACULTY BOOKLET

GLOBAL HEALTH:
NEUROLOGICAL AND
SENSORY DISORDERS:
GENES, PATHOGENESIS AND
INNOVATIVE THERAPIES
SEMINAR IN SALZBURG

March 13-19, 2022

A Global Educational Initiative by the
American Austrian Foundation



Wolfgang Aulitzky, MD

Director, Open Medical Institute
American Austrian Foundation

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Adjunct Professor of Clinical Urology
Adjunct Professor of Clinical Reproductive Medicine
Weill Medical College of Cornell University

Adjunct Professor of Pediatrics
**Perelman School of Medicine at the Children's Hospital
of Philadelphia**

Associate Professor of Urology
Medical University of Innsbruck, Austria

Wolfgang Aulitzky, MD is the Medical Director of the American Austrian Foundation. He is Associate Dean for International Medicine and Distance Learning, Adjunct Prof. of Clinical Urology and Adjunct Prof. of Clinical Reproductive Medicine at the Weill Medical College of Cornell University/New York Presbyterian Hospital. In 2016, he was appointed Adjunct Professor of Pediatrics in the Associated Faculty of the Perelman School of Medicine at the Children's Hospital of Philadelphia. He is also Associate Prof. of Urology at the Medical University of Innsbruck and Visiting Professor at the Medical University of Vienna. Amongst others he is a member of the American, German and Austrian Societies of Urology and was awarded the Zuckermandlpreis of the Austrian Society of Urology in 1989. In 1995 he received the Silver Medal, in 2007 the Golden Medal for Merits to the Republic of Austria and in 2014 the cross of honor of the Land Salzburg. As Director of the Medical Program of the American Austrian Foundation he has initiated the Open Medical Institute, a scientific and educational collaboration of Weill Cornell and the New York Presbyterian Hospital, the Children Hospital of Philadelphia, Duke University, Columbia University, the Cleveland Clinic and leading hospitals in Austria. Dr. Aulitzky earned his medical degree at the University of Innsbruck in 1977, was a research associate at the University of Uppsala, Sweden and the Rockefeller University, New York. He received his training as an urologist at the University of Innsbruck and the General Hospital of Salzburg. He is the author of more than 140 publications on Urology, Andrology and Health Care issues and is co-author of books on basic and clinical urology/andrology.



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Aziz El-Amraoui, PhD joined the Institut Pasteur (Paris) after a PhD in Neuroscience from the University of Lyon-I in 1995, where resorting to dozen identified deafness genes as entry points has enabled him to enlighten both fundamental and medical aspects of hearing & vision functioning and related disorders (<https://orcid.org/0000-0003-2692-4984>). Multidisciplinary and multiscale approaches owing to the biochemical properties of the encoded proteins, identification of their molecular networks, deep-phenotyping of related animal models have provided major cues for understanding how the inner ear & eye sensory organs develop and function (Jean-Valade Prize 2005, Fond Mazet-Danet Fondation de France, 2006; Chaire of Excellence Charles Nicolle, Institut Pasteur (2017). Building on accurate and well-documented disease pathogenic mechanisms, his team current efforts are focused on late-onset and/or progressive hearing and vision impairments, from pathogenesis to treatment solutions. The major aims of the team are to i) elucidate the origins of disease progression and severity, and ii) identify therapeutic targets and solutions to delay, prevent and/or cure sense(s) deterioration in animal preclinical models, in anticipation of future transfer into clinics.



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Isabelle Audo, MD, PhD is a clinician scientist, professor in ophthalmology, working both at the Quinze-Vingts Hospital and as a group leader in the Department of Genetics at the Vision Institute (Institut de la Vision) in Paris, France. Her areas of expertise are medical retina, inherited retinal disease both for clinical and molecular diagnosis, and visual function explorations with clinical electrophysiology and imaging techniques. Pr. Audo went to medical school at Paris XI University where she received her M.S. degree in Immunology. She completed a residency program in Lille (North of France) from 1994 to 1997, where she became particularly interested in surgical and medical retina, especially in retinal dystrophies and clinical visual electrophysiology. Following her residency, she earned a Master degree in Cellular and Molecular Biology at Louis Pasteur University in Strasbourg, France with Pr. Sahel, and then in 1998, earned her M.D. Pr. Audo completed a research fellowship from 1999 to 2003 at the Department of Ophthalmology and Visual Sciences, University of Madison, Wisconsin, with Pr. Albert, and earned her Ph.D. From 2003 to 2005, she completed a medical retina fellowship under with Prof. Bird and Holder at the Moorfields Eye, Hospital in London. She went back to Paris, France in 2005 where she completed another Master degree in genetics. As a clinician and a scientist, Pr. Audo has developed a comprehensive expertise on inherited retinal diseases from the clinical diagnosis, patients' care to translational and more basic research aiming at a better understanding of the pathogenic mechanisms underlying these disorders. Pr. Audo's research on inherited retinal diseases has been published in more than a hundred scientific papers. She is also the coordinator of several laboratory and clinical research projects. She is the president of the Francophone genetic ophthalmic society and became in September 2021 the coordinator of the National reference center for Rare disease of Quinze-Vingts hospital and became the deputy director of the Institut de la Vision.

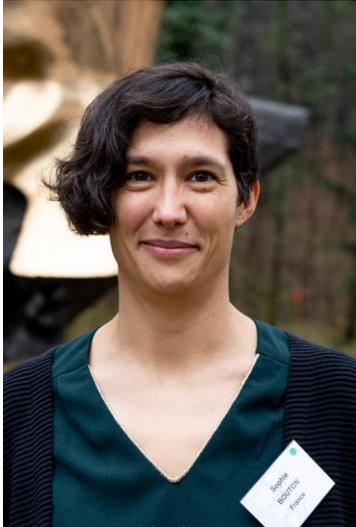


Paul Avan, MD, PhD

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Paul Avan, MD, PhD is both a physicist and a MD in biophysics, developed complementary skills to design original objective methods of exploration of the cochlea and auditory pathways. These methods have been validated on models of mutant mice with precisely defined molecular deficits that affect specific parts of their auditory system. The study of such models bridges the gap between two domains that shared few common knowledge two decades ago, audiology and molecular physiology. Once validated, the audiological tests developed by Paul Avan, currently head of the CERIAH (Center for Research and Innovation in Human Audiology at the Institut de l'Audition, center of Institut Pasteur in Paris, France) have been applied to diagnosis in patients, and to the design of novel electrophysiological equipment detecting formerly inaccessible parameters, such as hydrostatic pressure of labyrinthine fluids. For this purpose, Paul Avan has contributed to the creation of a company, Echodia (Electronique du Mazet), which builds and sells CE-marked equipment. Paul Avan's clinical duties during his career in a University Hospital (1992-2021) went from audiological exploration of patients, with equipment just transferred from bench to bedside, to the fitting of cochlear implants in profoundly deaf children and adults.



Sophie Bouton, PhD

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Sophie Bouton, PhD is a CNRS researcher working at the Institut de l'Audition in Paris where she studies the neural bases of speech and language. Sophie Bouton first completed a PhD in cognitive psychology at the University of Aix-Marseille, where she studied the cognitive mechanisms involved in speech perception in deaf children with cochlear implants. Her work has led to major results: she has shown that the auditory performance of children implanted before the age of 3 is more affected by the coding strategies of the acoustic signal than by the age of implantation. This discovery offers the opportunity to develop new therapies based on the training of afferent cortical pathways. She then pursued a post-doctoral career, first at the ENS in Paris, then at the Campus Biotech in Switzerland (University of Geneva) and finally at the Integrative Neuroscience & Cognition Center (University of Paris). She has been involved in several innovative projects that have led to publications in major journals in the field, including PNAS. Now recruited at the CNRS, Sophie Bouton uses the different techniques available for human brain research to restore speech function in patients with acquired disorders. To restore speech, she uses real-time neural activity decoding techniques and mathematical algorithms to convert neural activity into a speech signal. Sophie Bouton also uses similar neuroimaging techniques to study language acquisition. She uses the developmental course of language acquisition to extract patterns of functional connectivity between brain areas that would reflect periods favorable to learning. Her objective is to propose targeted neural therapies in response of neurodevelopmental disorders to preferentially activate specific networks or mechanisms at the right time of acquisition.



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Deniz Dalkara, PhD is a tenured research director at INSERM, France and leads a team on gene therapies and animal models of neurodegenerative disease at the Vision Institute in Paris. She graduated from Middle East technical University with a B.S. degree in Biology in 2001. Afterwards, she obtained a master's degree in pharmacology and pharmacochimistry in Strasbourg, France where she later pursued a PhD degree in cellular and molecular aspects of biology. She was awarded the Biovalley PhD thesis award for the protein delivery method she developed during her graduate studies, which was subsequently commercialized under the name "Pulse In" by Polyplus transfections. Later she conducted her post-doctoral studies in the laboratory of Ernst Bamberg at the Max Planck Institute of Biophysics before moving on to UC Berkeley to do a second post-doctoral training in 2007. At UC Berkeley, Dr Dalkara applied viral engineering principals to enhance AAV vectors for their application in retinal degenerative diseases. Her work includes molecular evolution and engineering of viral gene delivery vehicles and their application to develop innovative gene therapeutic strategies to combat blinding diseases of the retina in mouse models of disease. In 2012 Dr Dalkara received the Young Investigator award to start her group at the Vision Institute in Paris. Since then, she's been recognized as an 'Innovator under 35' by the MIT Technology review and has been awarded Euretina and Paris Region innovation award. She created a startup company in 2020 which is now part of SparingVision. Since 2021 she is the part time chief scientific officer of SparingVision alongside her academic activities. She continues to carry out her research activities at the Paris Vision Institute with a strong focus on translational research.



Kate Grieve, PhD

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Kate Grieve, PhD is an INSERM Research Director and team leader at the Institut de la Vision, and Scientific Director and co-founder of the Paris Eye Imaging unit at the Quinze Vingts National Ophthalmology Hospital. Her research involves the development and application of high-resolution ocular imaging technologies, both for in vivo use in patients and for live imaging of cells in the lab. She is a leading specialist in both full field optical coherence tomography and in adaptive optics technology. Originally from Scotland, she obtained her undergraduate degree in physics from Imperial College London, followed by a PhD with Claude Boccara in biomedical optics at the Langevin Institute, Paris and spent time as a postdoc with Austin Roorda at UC Berkeley and Martin Booth at Oxford. In addition to her academic activities, she has worked in industry, commercializing innovative retinal imaging technologies, and recently created a startup named SharpEye. She is an associate editor of the journal Biomedical Optics Express and chairs the annual ocular imaging conference “i2eye”. She has been funded by ANR, ERC, FFB and IHU grants, and in 2020 was awarded a prestigious 5-year ERC Consolidator Grant to develop optical imaging of retinal structure and function in the context of gene and cell therapies.



Sandrine Marlin, MD, PhD

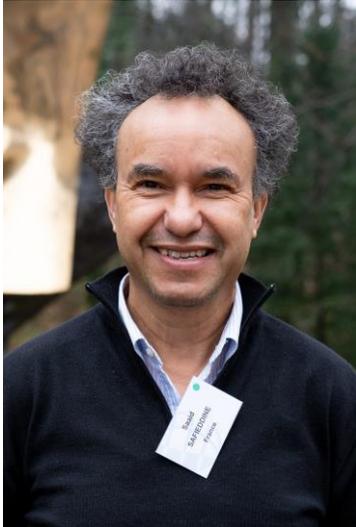
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Sandrine Marlin, MD, PhD is a clinical geneticist and researcher in the field of genetic hearing impairment. After a medical genetic MD, she underwent fundamental researches on deafness genes identifications in Institut Pasteur (Paris) during a PhD and a postdoc position. Since 2004, she coordinates in Necker's Hospital (Paris) a french network of 22 reference centres (Centre de Référence Maladies Rares Surdités Génétiques) associating clinical geneticists; molecular biologists; ENTs and researchers in the field of genetic hearing impairment. Since 2017, she also coordinates a similar European network and the part dedicated to hearing loss in the "Filière de santé maladies rares Sensgene", a network of all the reference French centres for rare Sensorial diseases. To date, she is the head of team located in Imagine Institute (Paris) which aims are to identify new genetic mechanisms responsible for rare hearing impairments (<https://orcid.org/0000-0002-4115-9806>). Involved in improving the lives of patients affected with rare genetic diseases, she co-directs the social actions of Imagine Institute.



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Saaid Safieddine, PhD has been active in the area of auditory physiopathology research for almost 30 years now. In the 1990's, Saaid Safieddine spent seven years as staff scientist in Robert Wenthold's laboratory at the National Institutes of Health in Bethesda, Maryland, USA. During that time, he made a determinant contribution toward the elucidation of the molecular architecture of the auditory hair cell synapse. In the late 1990's he joined the Pasteur Institute in Paris, wherein he has been working during the last 19 years. His achievements during that time have had still greater impact on our understanding of the molecular anatomy and function of hearing organ. In addition to pursuing pioneering basic research aimed at understanding the molecular genetics of hearing and deafness, Dr. Safieddine's recently started a translational research project focusing on the development of innovative therapies for deafness, especially gene therapy. His team conducted several proof of concept studies demonstrating for the first time that not only gene therapy can prevent deafness, but that it can also treat it once installed. These studies are raising new unexpected hopes for gene replacement therapy in deaf patients and open the way to future clinical trials. Safieddine's team is one of the three investigators of the University Hospital Research Project (RHU) AUDINNOVE. The goal is to develop gene therapy for one of the most frequent form of congenital deafness. This project has been selected for funding under the French State's Major Investment Programs involves tight collaboration between Dr. Safieddine's team and ENT clinicians at the Necker Hospital of Paris (Necker-Sick Children Hospital, Public Assistance - Hospitals of Paris).



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Séverine Samson, PhD is a cognitive neuropsychologist and a professor of Psychology at the University of Lille in France. After her Ph.D. in experimental psychology at the McGill University (Montreal) in 1989 and 3-year post-doctoral research at the Montreal Neurological Institute with Dr. Robert Zatorre, she took on a faculty position at the University of Lille and was nominated in 2008 and in 2014 senior member at Institut Universitaire de France. While maintaining clinical activity in Neuropsychology in an Epilepsy unit (Pitié-Salpêtrière Hospital, Paris), she developed neuropsychology training programs at the University of Lille, creating in 2002 a master's degree specialized in cognitive rehabilitation and in peri-surgical neuropsychological evaluation. Her research focuses on auditory perception, memory and emotion in musical and non-musical domains using methods taken from psychophysics, cognitive psychology and neuroimager. More specifically, she used music as a framework for understanding the functioning of human memory and emotions. This evolution has led her to experimentally investigate potential therapeutic applications of music in the rehabilitation of cognitive and affective neurological disorders. The multi-disciplinary approach used combines clinical research with the experimental rigor of basic research, at the interface of art, science and cognition. With the support of 25 international research grants, these studies gave rise to 155 peer-reviewed papers or book chapters. Finally, as a member of the International League Against Epilepsy on three occasions, she contributed to several reports on indications and expectations for neuropsychological assessment in epilepsy care and participated in several international courses. Prof. Samson is currently on the Faculty of Psychology (Univ Lille) and La Pitié-Salpêtrière Hospital (Paris) where she is doing clinical research on auditory processing at the Paris Brain Institute (ICM).

Fellow Booklet
**Global Health: Neurological and Sensory Disorders:
Genes, Pathogenesis and Innovative Therapies**



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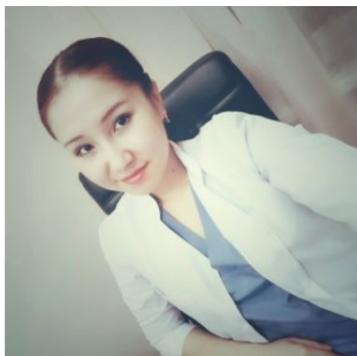
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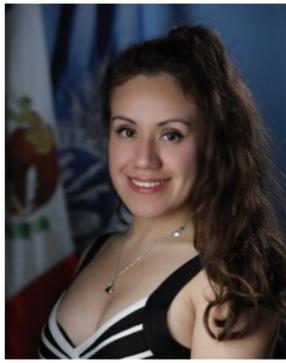
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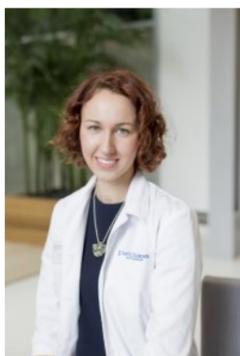
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DIARY



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Sunday, March 13, 2022

It was a lovely sunny Sunday. I enjoyed driving over the snow-covered Alps. When arriving to Salzburg, I was immediately immersed in a friendly atmosphere, which I missed over the last two years. The pandemic is hopefully showing the last of its strength and, despite wearing the masks, one could easily feel the friendly, warm welcome from colleagues who came to Salzburg to learn about neurological and sensory disorders and the novel therapies in rare diseases. Prof. Wolfgang K. Aulitzky (OMI CEO) and Prof. Aziz El-Amraoui (course director) introduced the main topics as well as the practical and scientific organization of the course. We were very excited about the content, which was to be presented from the scientific, research, as well as clinical point of view. At dinner we were talking about our everyday life. During COVID-19, we clinicians shared the same problems and were trying to find solutions. It was interesting to hear that a Belarus colleague was vaccinated twice with Sputnik, once with Janssen, and the fourth time with Pfizer. It was evident that Eastern Europe had different vaccination strategies than the West. We also could not avoid commenting on the tragical war in Ukraine. We hope that it ends soon.

Monday, March 14, 2022

At 8 o'clock we took the pre-seminar test. It was a really difficult test. I realized that some of these topics were covered when I studied for my PhD. However, this motivated me to listen carefully to the topics. I reassured myself that the answers would be discovered later during the week. The introduction and the first lecture was given by Prof. El-Amraoui. He presented on the Institut Pasteur. Luis Pasteur said, that: "science knows no country, because knowledge belongs to humanity, and it is the torch which illuminates the world." Prof. El-Amraoui walked us through the secret life of the inner ear and how it works. I was impressed by the simple way he clearly explained such a complex issue. When he started to show the ontogenesis of the inner ear, I was reminded of my biology classes, which I loved and is why I decided to study medicine. Then, Sophie Bouton presented on augmented reality and brain-computer interface. It was amazing to see videos of use of technology which was not possible some years ago. At the round table, we discussed the concept of open science. It is difficult to access the international journals if your financial resources are very limited. Hence information about the "free" scientific data was warmly welcomed. However, we live in times where everyone is overloaded with data. We also discussed the importance of a critical mind and the problem with trustworthy information. In the afternoon, Ms. Stephanie Faschang gave us a lot of information about the OMI. It is philanthropic organization which gives the opportunity to young doctors who would like to advance their knowledge. I am very grateful to have had the opportunity to be here because I have learned so many things. I became a much better doctor and a better person because of these seminars. The day was over before we knew it. A friendly atmosphere and opportunity to ask questions helped me to understand and remember the given information better. After dinner, we strolled around the city and enjoyed more of Salzburg's night atmosphere at a local pub.

Tuesday, March 15, 2022

In the morning, Sophie Bouton concluded the lessons about the augmented cognition. This time we proceeded with brain implants: cochlear implant and novel therapies like tACS and tDCS for dyslexia. Then, Isabelle Audo presented about vision. One could just see how she loves her work. She took us on a journey through the eye and the layers from optic fibre to pigment epithelium, from rods to cones. Afterwards, she covered blindness with special attention to the genetic causes, esp. retinal dystrophy. It was a very interesting section. After the coffee break, our attention was grabbed by a very energetic, clinical geneticist named Sandrine Marlin. I have never heard someone go through the genetic catalogue (with all those abbreviations, numbers) with such passion for genetic counselling for the patients. At the round table, some interesting ethical issues were discussed. We didn't even notice how time flew by. After dinner, we went for a short walk, as the weather was not nice. However, the rain could not stop our fun.

Wednesday, March 16, 2022

In the morning, animal and cell-based modelling and pathogenesis of blindness was presented by Deniz Dalkara. I enjoyed how she reasoned the animal models: from humanized mice to induced injury on healthy tissue. Prof. El-Amraoui led us then to hearing loss. It never occurred to me how severe this problem is in terms of public health. Personally, I think that the WHO should propose screening mechanisms for hearing loss after 45 years of age, just like the screening for colon, breast, and cervical cancer. It is important to understand the disease's mechanisms in order to adapt the best therapeutic option. We covered different usher types to

understand the hearing loss better. Paul Avan then took us from animal models back to humans with hearing and balance deficits. He explained it in a humorous way, that we all have remembered the logics behind measuring the effects on hearing. The afternoon was free, so we went for a walk. Some visited the Salzburg castle, others went shopping. The weather was unfortunately not so nice, so we could not enjoy the beautiful mountain panorama. After dinner, we had a long chat in the lobby. After two years of COVID-19, everyone is longing for time to relax and to enjoy small talk.

Thursday, March 17, 2022

In the morning, we enjoyed the lecture from Severine Samson about the emotions and cognition in hearing loss patients. In the afternoon, she gave a very comprehensive review on music interventions in elderly patients: from music therapy and dancing in patients with Parkinsonism, to music therapy in patients with Alzheimer's dementia. In my family, we all play an instrument because we think that music really opens the heart and helps the brain, too. I really enjoyed the lectures and was looking forward to the chamber music concert later on. Before the concert, we had to cover some basic research with Saaid Safieddine, who introduced us to genetic therapies and adenoviral vectors. Paul Avan was very practical as he reminded us of aging and the importance of listening to music of reasonable, but not too loud, sound. At the roundtable, some interesting topics were raised. Then we had a tasty dinner once again! I really enjoy the food here and the fact that I do not need to cook. In the evening, we experienced a lovely chamber music concert in Schloss Arenberg. A mellow violin with a cello was a perfect match! It was very relaxing. We enjoyed good music played by excellent musicians. After the concert, we had a drink and a long talk. During these days here, we got to know each other and shared not only medical experiences, but personal stories too. It is good to see that we are in some respects very much alike, but on the other hand, so different. This is what makes the scientific and medical community so interesting!

Friday, March 18, Friday

The last day was full of interesting lectures. First, we had a video lecture from Kate Grieve on imaging of the human eye. Then came my top lectures – Deniz Dalkara and Aziz El-Amraoui gave very comprehensive talks on genetic therapies in both sensory disorders: vision and hearing loss. It was very didactic, as I really had to think to understand. Then we had a round table and the post-seminar test. We were tested to see how much we had learned. I am sure everyone learned a lot. Looking back at the week, I was very happy because I found new friends, have learned a lot, and yet at the same time, I was a bit sad because the seminar was ending. However, I hope that in the future some of us will meet again and I will have the opportunity to attend more interesting and useful seminars like this one. I will look at the genetic therapy and sensory disorders with different eyes from now on! I want to express my great gratitude to everyone in the organization of this perfect, interdisciplinary seminar. I was given the opportunity to gain new friends, extending my network to an international level. I will never forget this experience. The most important thing was the daily exchange with other people made me grow as a doctor. I will surely suggest this seminar to my colleagues.



Andres Kamaid
Institut Pasteur de Montevideo
Uruguay

Saturday, March 12., 2022

I arrived in Salzburg at night after a long journey. This was my first trip since the COVID-19 pandemic started, and it turned out to be easier than expected. Moving around here was very simple and people in the street were very kind to help me get to my destination. My arrival was quite late at night, but Manuel was at the reception, and he very kindly received me. I was not expecting such a nice room, which was perfect for a much-needed rest

Sunday, March 13, 2022

Waking up was a delightful experience. I discovered through the window the wonderful landscape where Schloss Arenberg is located, I hadn't really noticed the night before. I went for a walk in the city, and the sunny Sunday allowed me to enjoy Salzburg's quiet atmosphere, which I loved. Lots of people were sitting next to the river, so I did as well for a while, listening to a street musician, and it felt like a wonderful welcome from the city. Later in the afternoon, Prof. Wolfgang K. Aulitzky was in charge of doing the same warm welcome on behalf of the OMI, and Prof. Aziz El-Amraoui and the faculty introduced themselves. We met Stephanie Faschang, who had helped us a lot for the pre-course process, and I was able to talk with fellows by sharing a drink in the lobby. I went to bed very excited about sharing the upcoming week with such a diverse group of people.

Monday, March 14, 2022

After a nice breakfast shared with a couple of colleagues from Brazil, Prof. Aziz introduced the Institut Pasteur and the Hearing Institute in Paris, as well as presented the general idea of the course. Then, we took the initial test, which I found difficult, since many questions were not part of my expertise. However, it provided a good overview about what was coming. Also, it elicited some interactions during the coffee break since many fellows were curious to know if we had the same feeling. The first lecture by Aziz was a wonderful recap about all the complexities of audition and balance, and the link with evolution. Despite being a familiar topic for me, his wide perspective about all the processes described was very enlightening. After lunch, Zilton from Brazil gave a case presentation, which brought up some challenges faced by healthcare systems in the developing world, including management of rare diseases. Then, Sophie Bouton began a series of lectures about a fascinating topic which I knew very little about, machine-human interfaces and devices. Although it sometimes felt like I was seeing a science fiction movie, I believe she did an amazing job in explaining the fundamentals behind amazing examples of brain-computer interfaces, and summarizing the current knowledge and challenges, with varied examples. Then the round table promoted very interesting discussions about open science and neuro-sensory precision medicine. As a strong promoter of open science, I found it very important to have raised this issue in the course. Finally, the presentation of the OMI by Stephanie Faschang was helpful to better understand the uniqueness of this experience. I loved the concept of “preventing brain drain, promoting brain gain”. Afterwards, an evening walk with several fellows around downtown Salzburg was perfect to relax and continue conversations about the day. We had a nice beer with some local delicacies in a very welcoming pub.

Tuesday, March 15, 2022

In the morning, Sophie Bouton continued with a very interesting lecture more focused on deafness and dyslexia. She explained in a very accessible way all the steps involved in cochlear implant developments, and I learned interesting facts about dyslexia and its links with sensory processing in the brain. I also feel that after her talk I could understand more deeply how cochlear implants work and what the challenges for improving them are. Next, we moved to a different sensory modality: vision. Again, the ability of Isabelle Audo to cover a very complex topic, such as how the eye works, was incredible. She explained cellular, molecular, and basic neurophysiology in a detailed way, even for a basic neuroscientist like me. However, she managed to be very clear for the whole audience, as we discussed with clinician fellows during the coffee break. Her following talk was more oriented to clinical aspects of blindness, which was very useful for me to understand how alterations of eye development or function translates into clinical problems, something completely new to me. Similarly, the talk from Sandrine Marlin provided us all with a comprehensive catalogue of genetic problems affecting audition. I found both talks to be great examples of integration of basic research and clinics. In our Uruguayan community, it is not easy to find clinical doctors with such a deep understanding of basic research, so it was very inspiring. During the round table, interesting discussions were generated about ethical issues as well as an interesting perspective about the clinical practice when dealing with genetics, counselling, and management of rare diseases. After dinner, once again, we enjoyed the fresh and quiet environment of the city, this time with a different group of people.

Wednesday, March 16, 2022

The morning presentation by Deniz Delkara gave us an amazing perspective on the different strategies to research innovative therapies for blindness. In a very interactive and clear way, she covered thoroughly the different models currently used, promoting discussion about their pros and cons. Similarly, Aziz El-Amraoui approached the same issues but for hearing disorders, so we could clearly understand differences and similarities. After lunch, we learned from Paul Avan, who provided extraordinary examples of the concepts talked about in the morning. He also explained very clearly how their work with animal models could lead to the identification of the cause of hearing loss. During the free afternoon, while drinking a nice espresso coffee, I had a more in depth talk with Dr. Aulizky about the OMI, which was very interesting for me to think about the future possibilities for our Uruguayan community. Unfortunately, I could not go sightseeing with my other fellows, as I stayed in my room finishing some work duties. However, I can say that Schloss Arenberg's peaceful and comfortable environment was perfect for that. At night, we went with many colleagues to a traditional beer house where we could interact and learn more about each other.

Thursday, March 17, 2022

Starting in the morning, Severine Samson gave us a nice perspective on a very interesting topic that I had very little knowledge on: hearing deficits and its relation with emotion and cognition. Then, Saaid Safieddine gave us a wonderful example about treatment solutions for hearing disorders, describing his ongoing gene therapy approach. Later, Paul Avan illustrated very nicely the importance of external factors in hearing. His enthusiasm and didactic capacity were very nice. After lunch, Severine Samson completed the panorama of the field of cognition and hearing, highlighting the importance of music for function and treatment, but also the difficulties for research in this. This was evident in the round table discussion, where active and interesting discussions about this topic were raised. In the evening, the chamber music concert was very touching for me. We had heard about music and its importance in brain function, which became evident at that moment. Afterwards, with a glass of nice wine, we stayed in the lobby talking with Aziz and others in a very relaxed and joyful atmosphere.

Friday, March 18, Friday

At 7:30 AM I met Kaitlyn, with whom I had exchanged several emails pre-course. Again, she was very kind and helpful, taking me and some colleagues to get the required PCR test for traveling. It was very nice to meet the people behind the scenes and be able to express in person the acknowledgement for their great job at organizing everything. Before going into the last session of the morning, I was already excited. This has been a terrific experience that exceeded my expectations in every sense. Right now, I can only wish to participate again and help other people from Uruguay to take part in an OMI seminar.



Clara Mendia
Institut Pasteur
France

Sunday, March 13, 2022

My flight arrived in the early afternoon, and finally getting to my room at the Schloss was very relieving after the journey. I was curious and excited about the week ahead, especially after reading the list of fellow names from all over the world. Later in the evening, we had a welcome reception and were able to meet some of the faculty and the CEO of the OMI. I think we were all moved by the significance of being together for an in-person event after the recent 'pandemic' years, yet naturally aware of the responsibility to still be careful and of course make the best of the experience ahead of us. We had our first dinner together and the group seemed great. I looked forward to sharing the week with them. It was particularly easy to connect with fellow Latin American attendees from Mexico, Uruguay, and Brazil.

Monday, March 14, 2022

After our first breakfast, we had an introductory talk by the course director, Aziz El-Amraoui, with some background on the Institut Pasteur that celebrates the bicentennial of Louis Pasteur this year. He also presented the Hearing Institute, now operating from a separate building outside the Pasteur campus in Paris. We sat for our pre-seminar test; the general feeling was that we all made some mistakes. However, it makes sense given that we come from quite diverse backgrounds. Some are doctors, some scientists. Even within groups, the doctors are ophthalmologists, ENTs, neurologists; and us scientists are working on very different models. Anyway, other than being stressful, the scope of the test was an indication of the wide spectrum the seminar would include. Our inaugural talk was given by Aziz El-Amraoui and he covered fundamental aspects of hearing and balance. He was very didactic and managed to keep us engaged despite the considerable amount of information. We saw the system from a physiological, genetic, and functional level. It was interesting that he also included an evolutionary perspective. Because my PhD project focuses on a gene involved in hearing and

vision, I have background on the subject, but it was still interesting to have a comprehensive overview before diving deeper in the following days. For the afternoon lecture, my feeling was quite different. Sophie Bouton talked about brain-computer interfaces, a topic that I didn't know in depth, nor do I think the rest of the group did. However, she was able to introduce us to the concepts, applications, and challenges of this very innovative field.

Tuesday, March 15, 2022

The day started with another lecture by Sophie Bouton, this time about brain stimulation as a treatment for deafness and dyslexia, which was followed by two expositions by Isabelle Audo about the physiology of vision, and from a more clinical angle, about blindness. After lunch, we transitioned from blindness to deafness with Sandrine Marlin's lecture. Because I am familiar with mouse models of deafness, it was super interesting to see the parallels with the clinical presentations in humans and the reality of the patients that our research ultimately aims to help. The day ended with a round table on genetic diagnosis of rare sensory diseases and genetic counselling. The exchanges between the attending physicians and the faculty were very engaging and it was an opportunity to analyze the differences in the protocols among their different countries of origin. In the evening, some of us went to visit the city center and tried some local cuisine. We had a great time and got to know each other better.

Wednesday, March 16, 2022

The first lecture was by Deniz Dalkara on blindness, disease modelling, and pathogenesis. I had been looking forward to her contribution and was not disappointed. The talk was very dynamic, and a lot of open questions were raised. Such questions were not only central to my research project, but to some of hers as well. Her presentation included key publications on innovative gene therapy strategies and examples to the advantages and limitations of different cell and animal models. An important takeaway was the idea that it is vital to consider the limitations of each model and design the project accordingly. In my case, this means that we will complement in vivo and in vitro models. Next was a lecture by Aziz El-Amraoui, provided similarly to the previous one, but for hearing loss modelling and pathogenesis. This underscored the importance of his previous talk by giving an overview of the system, as we now focused on genes and their mutations' effect on phenotype. Though we tend to individualize genes to study their function, or when designing therapies to target monogenic diseases, it was worth noting that in their normal function they interact in ways that can be complex to elucidate. This lecture paired nicely with the next, which was by Paul Avan. He focused on the translation from animal models to humans, and how different models -namely point mutations and knockouts- can help us understand the molecular mechanisms underlying disease manifestation. I was very impressed by the work he showed on pejvakin deficit, a study with not only scientific challenges but also difficulties in reaching and testing patients living in remote, isolated regions under geopolitical instability.

Thursday, March 17, 2022

Our first lecturer, Séverine Samson, brought us a very different perspective to what we had been focusing on. Her work on the connection between cognition, emotion, and hearing loss highlighted how complex the interconnection between these processes is. It was very striking to see what an important contribution hearing loss during mid-life can have on the risk of developing subsequent dementia. We transitioned from this discussion to talking about treatment solutions with Saaid Safieddine. He took us through possible approaches and factors to consider for gene therapy strategies and went into some detail for a couple particular genes his lab has focused on. It was particularly interesting to see the different windows of intervention they tried (on mice) and what their equivalent would be in terms of the human lifespan. Specifically, I was glad to see that they were able to have some function restoration even when intervening at adult stages, something that is still an important challenge in these kinds of studies. We then had another lecture by Dr Avan, now adding an additional layer to our mostly gene-focused lens so far: the contribution of aging and environmental factors to hearing loss. He was able to convey the relevance of this dimension for patient analysis, animal modelling - and to what point it will follow the equivalent process in humans - and even for our own awareness about preventing modifiable risk factors such as sound exposure or being diligent with auditory check-ups. A striking highlight was that current standards in audiometric testing could be improved, since there are deficits that can go undetected for a considerable time. Of course, this can apply to our testing of hearing function in mouse models. We had Séverine Samson again for our afternoon lecture on musical interventions for neurological disorders. This topic is far from my area of expertise, but she shined light on a set of study design issues that I think are widely applicable and important to keep in mind regardless of the subject matter. The day ended in the most memorable way since we attended a chamber music concert by French and Mexican performers. It was very enjoyable and in line with the host city's character.

Friday, March 18, Friday

The final day is here! What an intense but rewarding week it has been. We started the day with our only virtual lecture, by Kate Grieve, joining us from the US. She gave an overview into the workings and innovation on eye imaging technology, both for essential and cutting-edge techniques. The rest of the day had a clear therapeutic/translational focus, lectures by Dalkara and El-Amraoui, as well as a very engaging round table. It was a good way to integrate what we have seen throughout the week and leave us with open perspectives from here on. Once we were through with the post-seminar test and final discussions, we proceeded to a lovely farewell reception and dinner. It was bittersweet to say goodbye, but we will look back fondly on this experience. I take home very informative points raised by the basic investigative but also the translational lectures. It was my first experience with such a rich interaction between the clinical -diagnostic and curative- and basic research perspectives. I look forward to seeing the open questions we discussed explored and answered in the following years.



Rahma Mkaouar
Institute Pasteur of Tunis
Tunisia

Saturday, March 12., 2022

I arrived to Salzburg by plane at almost 9 PM, coming from Frankfurt because there was no direct flight from Tunis, where I live, to Salzburg. I was very tired but at the same time very keen to participate in the seminar. While I was on the bus heading to Schloss Arenberg, I caught a glimpse of the city and found it to be extremely beautiful. I really loved Schloss Arenberg and its surrounding greenery with abundant trees. After checking in, a very gentle and friendly receptionist provided me with important information about the first day of the seminar, then I settled down in a very nice and comfortable room.

Sunday, March 13, 2022

During breakfast, I met a very nice neurologist from Uzbekistan. I went for a little tour in the city, which was indeed amazing, calm, and full of friendly people. At 7 PM, we all gathered in the hall for the welcome reception. Prof. Wolfgang K. Aulitzky (CEO of the OMI) and course director Aziz El Amraoui described the main topics and the different organizational aspects of the course. At dinner, I met two PhD students from Italy and another from France with whom I had a very nice conversation.

Monday, March 14, 2022

At 8 AM, Aziz El Amraoui welcomed us to the seminar again and we took the pre-seminar test. I found the questions related to cognitive rehabilitation using artificial intelligence difficult, but I did not worry about this since I was attending this course in order to gain insights about different techniques and emerging therapies related to neurosensory diseases. The first lecture was presented by Aziz El Amraoui and it was about the anatomy of the ear as well as the physiology of the cochlea and the vestibular system. Aziz El Amraoui also explained the impact of evolution on development and the function of the inner ear. I really liked his presentation and I found it very well structured and pedagogic. I think that as a PhD student working on the genetics of hearing loss, acquiring more knowledge about the pathophysiological mechanisms involved in hearing loss would help to interpret more accurately the molecular results I obtain in my daily practice. The afternoon lecture was presented by Sophie Bouton, and it was about the emerging technologies used to rehabilitate patients suffering from neurological and neurocognitive disorders. Afterwards, we participated to a round table in which the professors presented new tools and software used for *in silico* analysis, as well as websites that give free access to articles. After the round table, Ms. Stephanie Faschang gave us a presentation about the OMI, its aims, and all the opportunities offered by this foundation to young doctors. I also enjoyed the lunch and dinner breaks because they were an opportunity to make connections with other fellows and learn more about their different specialties and experiences.

Tuesday, March 15, 2022

In the morning, Sophie Bouton presented the first lecture which was about the AI technologies used for deep brain stimulations. It was very interesting, especially because she presented several videos to better comprehend the outcomes of these techniques. The lecture was presented by Isabelle Audo who gave an extensive insight about the anatomy and physiology of the eye. After lunch, the first session was about the different forms of deafness. I found it very interesting, and it helped me to deepen my knowledge about the clinical characteristics and the different molecular aetiologies of hearing loss which will evidently help me in my research. Next, we had a round table about the genetic counselling for neurosensory diseases. I found it extremely interesting because this subject is at the core of my research. Several points were raised, mainly the relevance of genetic counselling for deaf-blindness syndromes as well as the social and ethical considerations of genetic counselling for different disease categories. After dinner, my new friends and I went for a walk in the city center of Salzburg.

Wednesday, March 16, 2022

In the morning, Deniz Dalkara and Aziz El Amraoui presented two lectures about animal models and cell-based modelling for blindness and hearing loss. The two lectures were very interactive, and we were able to interrupt the professors and ask them questions. I learned a lot about the advantages and limitations of the different gene therapy approaches. Following these lectures, I became more aware about the importance of an accurate and comprehensive genetic characterization of deaf-blindness disorders, such as Usher syndrome, to perform gene replacement and editing therapies. After the coffee break was Paul Avan's presentation about phenotyping of different hearing loss and vestibular system anomalies by extrapolating these deficits in animal models. We then had a free afternoon, during which I had the chance to make a tour in Salzburg with my new friends.

Thursday, March 17, 2022

In the morning, Séverine Samson did a lecture about the link between the cognitive function and acquired deafness/presbycusis. She outlined the different risk factors of dementia as well as the importance of hearing aids in improving the cognitive function. She also explained the drawbacks of hearing loss on the emotional processing. Afterwards, Saaid Safieddine did a lecture about treatment solutions for hearing loss. He mainly focused on the beneficial outcomes of gene replacement therapy in mouse models using adeno-associated viruses to cure autosomal recessive hearing loss related to *OTOF* gene and inducing a peripheral auditory neuropathy. I really enjoyed this lecture because it made me realize the importance of an extensive knowledge of disease mechanisms underlying the different forms of hearing loss. This would be crucial for effective strategy planning and results interpretation of gene therapies. After lunch, Séverine Samson gave us a presentation about music therapy for neurological disorders and showed a series of videos of patients participating to controlled clinical trials. We could see the benefit of non-pharmacological treatments, namely music, on mood enhancement, stress, and other behavioural changes. After dinner, we attended a wonderful chamber music concert in Schloss Arenberg.

Friday, March 18, Friday

During the morning session, Kate Grieve presented her lecture from the USA via a live streaming platform. It was about the effective technologies used nowadays for the human eye imaging. Then, Deniz Dalkara presented a lecture on gene therapy for blindness. She mainly focused on how to develop efficient treatment solutions. By asking questions and interacting with the class, Deniz Dalkara depicted several benefits and disadvantages of different gene therapy approaches. I really liked her presentation style because it helped me to understand the logic behind every gene therapy technique. Aziz El Amraoui followed with another lecture about the advances of gene therapy in hearing loss. He exposed the good outcomes, the limitations, and the current perspectives for improving cochlear implants. He then talked about the ongoing pre-clinical trials of gene replacement/editing therapies as well as optogenetics. In the afternoon, after the round table, we had the post-seminar test, which I found much easier than the first time, thanks to the great amount of information I acquired during this seminar. In the evening, we had the farewell reception and graduation dinner during which I had a great time with my new friends and discussed different topics of the course. I was very glad that I found new friends and have learned a lot. I hope that in the future I will have the opportunity to attend many more interesting seminars like this one. Finally, I want to express my great gratitude to the organization committee of this wonderful seminar.