REPORT ON THE 51ST EUROPEAN HUMAN GENETICS CONFERENCE, 16–19 JUNE 2018, MILAN, ITALY

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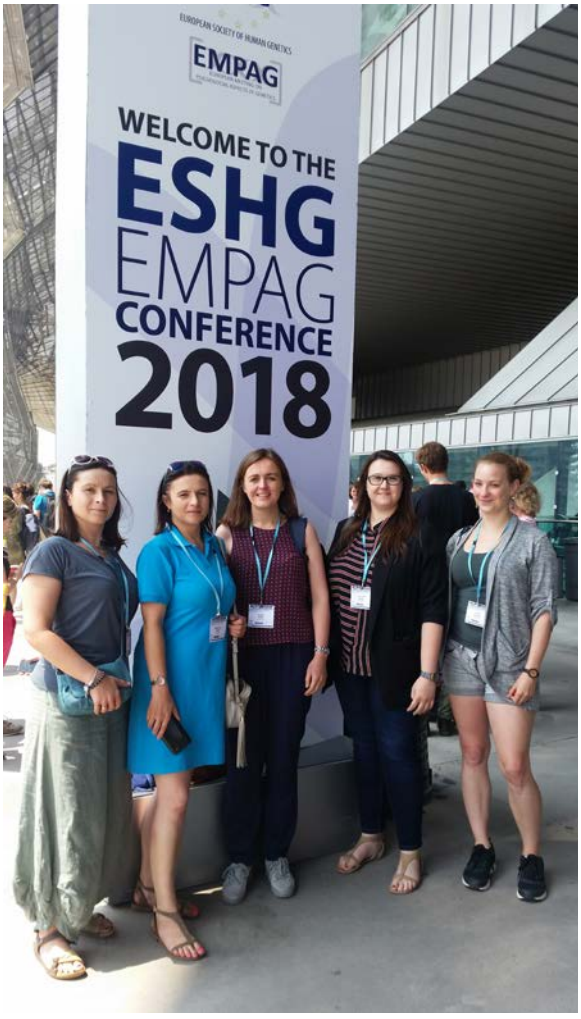
The 51th European Human Genetics Conference (ESHG 2018), in conjunction with the European Meeting on the Psychosocial Aspects of Genetics, was held on 16–19 June 2018 in Milan, Italy. The meeting was organised by the European Society of Human Genetics and, as every year, gathered people working on applied human and medical genetics from all over the world. Milan, the industrial capital of Italy, treasures its scientific tradition and offers the conference attender the unique opportunity to feel the spirit of the visionary genius Leonardo da Vinci. And so ESHG 2018 provided an exceptional conjunction of renaissance and contemporary science.

This year's conference attracted 3789 participants, making it the largest human genetics conference in Europe. Over four busy days participants had the option to listen to 93 hand-picked (invited) and 134 abstract-selected speakers, all of whom presented substantial discoveries in human genetics. The conference was divided into different sections: 5 plenary sessions, 23 concurrent sessions, 16 educational sessions, 19 concurrent symposia, 33 corporate satellites, and poster sessions. In addition, participants could also choose from 18 practical workshops.

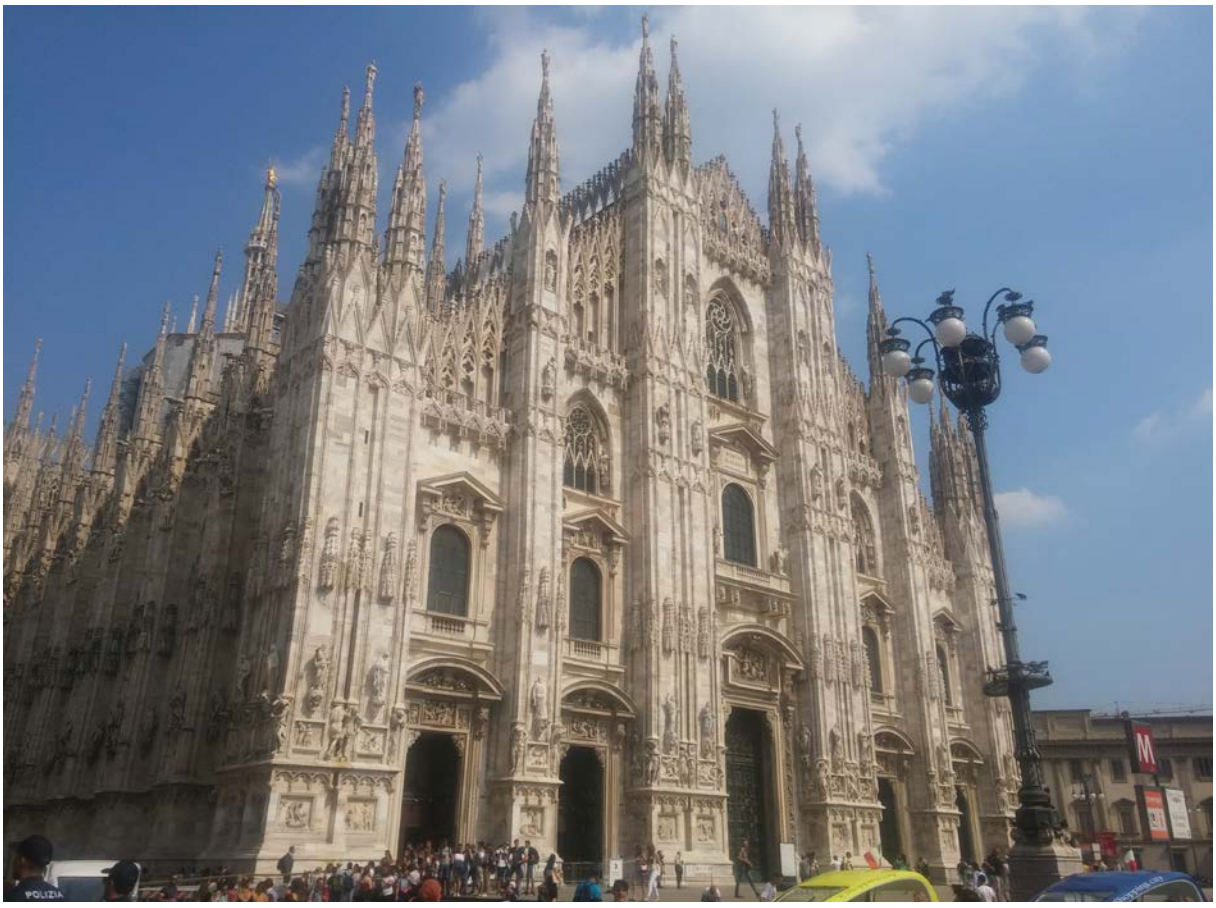
The poster sessions contained 1440 traditional posters and 497 electronic ones, structured into 20 topics. Within the exhibition area, 150 companies presented new technological and IT solutions, devices, and reagents. This year the commercial part of the conference was dominated by various solutions focusing on next generation sequencing technology.

Such a great variety of sessions made it difficult to choose the most interesting. To facilitate navigation between lectures and other activities, a dedicated mobile app (ESHG Society App) was available to participants free of charge. ESHG Society App was designed to guide delegates through the programme day by day, provide profiles of speakers and delegates, and seek out exhibitors by name or service provided. This modern solution allowed people to prepare their own personal plan, helping them to arrive at the right place at the right time.

The most exciting and prestigious part of the conference was the plenary sessions. Notable speakers, selected from renowned human geneticists, gave detailed reviews of major topics and state-of-the-art techniques. Opening the plenary session, the Leena Peltonen Prize for Excellence in Human Genetics was presented to Dr Tuuli Lappalainen, group leader at the New York Genome Center and Assistant Professor at Columbia University. Her research focuses on functional genetic variation in humans. Dr Lappalainen gave a talk on complex genetics, in particular integration of population-scale genome data with transcriptome and molecular phenotype data. This modern scientific approach promises to disentangle many intriguing issues in genetics such as the complex influence of coding and regulatory variants on the altered penetrance of causative variants, as well as a better understanding of the variation in gene dosage in the human general population and in individual patients.



The Institute of Physiology and Pathology of Hearing was represented by (from left) Anna Sarosiak, Dominika Ozieblo, Monica Oldak, Agnieszka Pollak, and Urszula Lechowicz.



Milan cathedral (or Duomo), world-renowned symbol of Milan, is one of the largest Gothic cathedrals in Europe

The second lecture in the opening session was given by Dr Serena Nik-Zainal from the Department of Medical Genetics, Cambridge, UK. She presented recent advances in the mutational signatures of human cells. The idea of mutational signatures sheds new light on the field of cancer genetics, providing a better understanding of the underlying sources of mutagenesis in the development of a tumor. In the near future this concept may become a cornerstone for new classifications and cancer therapies.

Beginning in 2006, each European Human Genetics Conference closes with a lecture by a distinguished speaker. It is named the Mendel lecture in tribute to Gregor Mendel, the forerunner of genetics. Perhaps this lecture might also be called a "Nobel lecture", since over the years six Nobel laureates have presented them. This year the Mendel lecture was given by Dr Emanuelle Charpentier, director of the Department of Regulation in Infection Biology at the Max Planck Institute for Infection Biology in Berlin, Germany. She presented a talk entitled "CRISPR-Cas9: how bacteria revolutionise genome engineering" and we must say that the title perfectly reflected the spirit of this innovative discovery. The CRISPR-Cas9 system was discovered during microbiological studies and recently emerged as a simple, precise, easy programmable and fast system of targeted genome editing in a variety of cells and organisms. Briefly, the bacteria capture fragments of DNA from invading viruses and use them to generate DNA segments called CRISPR arrays, which become specific "memory tags". During subsequent virus attack, the CRISPR arrays, together with Cas9 or similar enzyme, create precise machinery capable of cleaving the virus's DNA apart, thereby disabling the invader. This mechanism has been extended to a large variety of other cells and organisms, and holds great promise for future biotechnical and biomedical applications, including generation of transgenic animals and genetic modification of various eukaryotic cells. In the near future the CRISPR-Cas9 technology might possibly be applied to develop technology for treating serious human genetic disorders. It can be called a real breakthrough in the modification of genetic information.

The second part of the closing session was the ESHG Award Lecture, presented by Dr Matthew Hurles, head of Human Genetics at the Wellcome Sanger Institute, Hinxton, Cambridge. His talk, "Causes and consequences of new mutations", dealt with results of the Deciphering Developmental Disorders (DDD) study, the main aim of which is to elucidate the diverse genetic landscape of developmental disorders. DDD is based on a thorough and complex analysis of 14,000 children suffering severe, undiagnosed developmental problems. Combining different types of genetic data and state-of-the-art computational approaches, DDD's scientists and clinicians have a unique opportunity to identify new genetic disorders and decipher their molecular basis.

A number of sessions were devoted to otorhinolaryngology. A very interesting presentation dealt with the discovery of a new gene (*SLC9A3R1*) involved in age-related

hearing loss, relating it to functional studies on zebrafish and CRISPR-Cas9 technology. Another interesting talk was on the genetics of dizziness, elucidating the molecular links between migraine, vestibulopathy, and episodic ataxia. It presented the current state of knowledge on the genetic bases of Meniere's disease, highlighting that the disease shows clinical and genetic heterogeneity, so that both common and rare variants may help to shape a given patient's phenotype. Another talk summarised the cutting edge of hearing restoration via gene therapy, confirming the feasibility of applying Atoh1 gene therapy to the cochlea, although its success largely depends on the severity of the hearing loss. During a poster session, preliminary results were given of a study on the mechanisms of miRNA activity in chronic otitis media, as well as of an attempt to explore the genetics of cholesteatoma.

Another session summarised the results of several studies on genetically related hearing loss performed with next generation sequencing technology (targeted panels and whole exome sequencing). An interesting issue was a newly discovered candidate gene – *DIABLO* – for Meniere's disease (previously associated with autosomal dominant hearing loss). Next generation sequencing technology serves as a perfect tool for selecting new candidate genes in various diseases, including hearing loss, but there is a need to construct an effective workflow to confirm these discoveries. One such modern approach is based on whole exome sequencing followed by functional studies on animal models, and it was shown how this approach could be used to discover new genes related to hearing loss.

The Institute of Physiology and Pathology of Hearing was represented at ESHG 2018 by Monika Ołdak, Agnieszka Pollak, Urszula Lechowicz, Anna Sarosiak, and Dominika Oziębło. They presented five posters on various aspects of genetically related hearing loss within the session P02 – Sensory disorders (eye, ear, pain). In order, the posters covered (i) Evidence against *TMPRSS3*/*GJB2* digenic inheritance of hearing loss: practical lessons learned in the era of high-throughput sequencing; (ii) *CIB2* gene in the pathogenesis of hearing loss: results of pooled DNA high-throughput sequencing; (iii) Iterative sequencing and variant screening (ISVS) as a novel pathogenic mutations search strategy; (iv) First independent confirmation of the *PTPRQ* gene involvement in autosomal dominant hearing loss; and (v) First audiological characteristics of autosomal dominant hearing loss caused by a novel *TBC1D24* gene alteration. All the posters attracted interest from conference participants.

ESHG 2018 was a very exhausting meeting, with days starting at 8 a.m. and finishing at 8 p.m. or later. But it was really worth to be there! The next European Human Genetics Conference in planned for Gothenburg, Sweden, on 15–18 June 2019.