BRIEF SYNTHESIS OF THE COUNTRY REPORT HUNGARY

Report created in the framework of the project Promoters of advanced oncogenetics open online training and multimedia raise awareness on multidisciplinary assessment of patients and their families at risk of hereditary or familial cancer, Reference number 2018-1-RO01-KA202-049189, Strategic Partnerships for vocational education and training Erasmus+ programme

Molecular Genetics Department of National Oncology Institute, Budapest, Hungary

Specialist: Prof. Dr. Oláh Edit

It has been undergoing:

Department of Laboratory Medicine at the University of Debrecen, Hungary

Specialist: Dr. Balogh István PhD

Department of Medical Genetics at the University Pécs, Hungary

Specialist: Dr. Hadzsiev Kinga PhD

Department of Medical Genetics at the University Szeged, Hungary starting from 15. March. 2019

Specialist: Dr. Horváth Emese Ph.D; Dr. László Zsuzsanna Ph.D

Genetic tests and genetic counselling for hereditary cancers are available in Hungary however it is centralized in our capital Budapest. Universities of Debrecen, Pécs and Szeged need to establish and keep continuously maintaining a high-throughput diagnostic tool parks and oncogenetic counselling.

To reach our purpose there is a need for well-defined national funding system taking into account the increasing clinical needs and a good training program for an Oncological license exam with oncogenetic specifies or Clinical Genetic Board exam with special oncogenetic training.

Genetic testing related to inherited mutations of ***BRCA*** genes and risk assessment in framework of genetic counselling makes it possible to identify risk-

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averse people, thereby promoting early diagnosis, risk reduction, and proper therapeutic decisions.

***BRCA1* and *BRCA2* gene tests have been provided by the Molecular Genetics Department of National Oncology Institute, Budapest, Hungary for nearly 20 years** for families with hereditary defects in case of more than one breast or ovarian cancer on the same branch of the family or even one male breast cancer and also when the diseases are detected especially in young age (under 40 years). Genetic counselling and genetic tests are collaborated by a multidisciplinary team composed of clinical and molecular geneticists, clinical oncologists, breast surgeons, gynaecologists, human genetic assistants, psychologists in The genetic tests are financed by the Hungarian National Health Insurance Company.

Although there is a National Oncogenetic Healthcare in Budapest Hungary but decentralization of this unit is still missing, subsequently we would like to develop new Oncogenetic Healthcare Institutions at the tree other Universities too. Consequently there is further need for National Strategies for Diagnosis and Oncogenetic management of hereditary cancer patients. Diagnosis of hereditary risk for breast / ovarian cancer through BRCA genes and for familiar adenomatous polyposis through APC gene has already been performed in the non-capital Hungarian Universities at risk patients mainly in a context of scientific research, although the oncogenetic counselling is inevitable in these cases. The screening of hereditary, predisposition genes is currently a standardized practice in Western European countries, which allows personalised monitoring and genetic counselling for those at risk in these families.

We would like to improve the Hungarian Oncogenetic Healthcare in a following way: The necessity to decentralize the oncogenetic patient care in Hungary according to the increasing clinical need, to implement and develop Medical Oncogenetic Institutes and train oncogeneticists for genetic consultations. The long-term goal is to generate an oncogenetic expertise that will connect Hungary to similar European structures designed to monitor patients with hereditary cancer risk.

The need to identify and recruit patients with hereditary risk for monitoring: Hereditary Ovary and Cancer (HBOC), Hereditary Colorectal Cancer (HNPCC), Familial Adenomatous Polyposis (FAP). Patient identification will generate a consistent databases and a representative biobanks, according to the European normal

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and models, including clinical, epidemiological, morphopathological, moleculargenetic family history data. The information will contribute to complete the National Cancer Registry in Hungary.

The need for molecular testing of genetic risk factors (BRCA1, BRCA2, MMR, APC etc). The molecular genetic studies will need to include a pre-screening - dedicated and rapid techniques - of known, specific, recurrent or frequent mutations in the population and in particular, a full screening of mutations by complete gene or genome sequencing.

The need to interpret the results obtained, which will be at the basis of an epidemiological assessment of the risk factors for cancer in the Hungarian population. There are also no national approved risk assessment models available in Hungary.

Genetic testing of *BRCA1/2* genes in **the Department of Laboratory Medicine at the University of Debrecen** include targeted analysis of most common mutations by Sanger sequencing. The number of genetic tests performed in the **last 5-year period (2013-2018)** was **690**.

Department of Medical Genetics of University Pécs has started to carry out the *BRCA1* and *BRCA2* genetic tests. **Fifty** samples have been analysed in Pécs, Hungary until now. Beside the BRCA tests gene tests, **10 samples have been run around** for **RET proto oncogene**. One of our most commonly requested molecular tests is **Neurofibromatosis 1 gene** sequencing which have been conducted in **720 cases**; ***TSC1*** and ***TSC2*** have been examined in **150** patients.

Currently, they are in the process of optimizing the diagnostic workflow on both of their Next-Generation Sequencing instruments. (Human hereditary cancer panel: *BRCA1,BRCA2, PALB2, CHEK2, BARD1, BRIP1, RAD51C, RAD51D, TP53, MRE11A, RAD50, NBN, FAM175A, ATM, STK11, MEN1, PTEN, CDH1, MUTYH, BLM, XRCC2, MLH1, MSH6, PMS2, MSH2, 3' UTR of EPCAM)*.

Institute of Medical Genetics of University Szeged are going to establish the genetic test of *BRCA1/2* mutations starting from 15. March 2019.

Beside HBOS, Medical Genetic Institute of Szeged has been investigating the genetic backround of patients suffering from familiar adenomatous polyposis (FAP) since one year. Genetic screening in families with high risk to develop colorectal cancer (CRC) prevents incurable disease and permits personalized therapeutic and follow-up strategies. The advancement of next-generation sequencing (NGS)

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technologies has revolutionized the throughput of DNA sequencing. A series of probands for familial adenomatous polyposis **(FAP; 8 cases)** have been investigated for intragenic mutations of CRC familial syndromes-associated genes (*APC*, *MUTYH*, *MLH1*, *MSH2*, *MSH6*, *PMS2*, *SMAD4*, *STK11*, *PTEN*) applying Illumina Next Seq 500 NGS panel and conventional Sanger sequencing.

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