MPN&MPNr-EuroNet

Ex-COST Action BM0902 (2009-2013)

Description of MPN&MPNr-EuroNet

Philadelphia-negative myeloproliferative neoplasms (MPNs) are rare clonal diseases characterized by chronic elevation of blood cell counts (red blood cells, platelets, granulocytes), splenomegaly, and fibrosis of the bone marrow. There are three MPNs: polycythemia vera (PV), characterized by over production of red blood cells; essential thrombocythemia (ET), characterized by overproduction of platelets; and primary myelofibrosis (PMF), characterized by splenomegaly and fibrosis of the bone marrow.

In 2005, the discovery in Europe of the V617F mutation in the *JAK2* gene in the majority of MPNs has renewed interest in these diseases.[1] Since 2005, mutations in two other genes, *MPL* (2006) and *CALR* (2013), have been discovered in MPNs with no *JAK2*V617F mutation.[2,3] Consequently, new diagnostic tools have being designed to detect and quantify the *JAK2*V617F mutation, as well as the *MPL*W515L/K and *CALR* mutations characteristic of MPNs. In addition, several other genes have been described as mutated in MPNs, as well as in other hematological malignancies; some of the additional mutations may serve as pronostic markers. Similar progress has been made in the rare congenital/hereditary diseases related to MPNs (MPNr), such as congenital erythrocytosis (CE) and hereditary thrombocytosis (HT). Several genes have been described as abnormal in these diseases but the diagnosis of patients remain difficult and too often, not done.

In 2007, a group of European biologists decided to share their expertise in the new molecular assays designed to detect the mutations identified in MPNs and in MPN-related diseases. This informal network led to the first international comparative study of *JAK2*V617F assays, in an effort to harmonize the detection and improve the quantification of the main MPN mutation.[4] The new European network was made official as MPN&MPNr-EuroNet in November 2009 thanks to the creation of COST Action BM0902, funded by the Co-Operation in Science and Technology (COST) programme, until November 2013.

MPN&MPNr-EuroNet, now strong of 148 members representing 30 countries, fosters cooperation among European MPN experts to improve understanding of MPNs and related hereditary diseases and to facilitate and harmonize the diagnosis of these diseases in Europe. Each spring, MPN&MPNr-EuroNet organizes an international meeting, open to all. Since 2014, the network has been supported by the MPN&MPNr-EuroNet Fund, within the Project Foundation of the Université of Nantes, France.

Main achievements of MPN&MPNr-EuroNet

Since 2009 MPN&MPNr-EuroNet has optimized *JAK2*V617F assays and determined reference *JAK2*V617F standards. During the 2009-2012 period, joint collaborative studies between MPN&MPNr-EuroNet and European Leukemia Net led to the determination of the optimal *JAK2*V617F assays recommended for diagnostic use in Europe (Jovanovic *et al.*, 2013).[4] These studies indicated a strong need for reference materials to enable standardization of *JAK2*V617F testing and quantification (Lippert *et al.*, 2009; Asp *et al.*, 2017).[5-6] More recently, MPN&MPNr-EuroNet collaborated with the National Institute of Biological Standards and Controls (NIBSC, UK) to produce a panel of genomic *JAK2*V617F-mutated reference DNAs, which was approved in October 2016 by the World Health Organization (WHO) as the 1st WHO International Genomic Reference Panel for *JAK2*V617F, for both

mutation detection and quantification.[7] Regarding CE and HT, MPN&MPNr-EuroNet has centralized and organized the detection of the main CE- and HT- associated mutations, notably by using Next Generation sequencing (NGS). MPN&MPNr-EuroNet has also helped diffuse information about these very rare diseases, including via publications and reviews (Hussein *et al*., 2014; Bento *et al.*, 2014).[8-9] Thanks to COST funds, via one book dedicated to CE and HT. Finally, since 2009 MPN&MPNr-EuroNet has helped communication and exchange between researchers, biologists and clinicians via the organization of 12 international meetings dedicated to MPNs, CE and HT.

References

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