Research corner

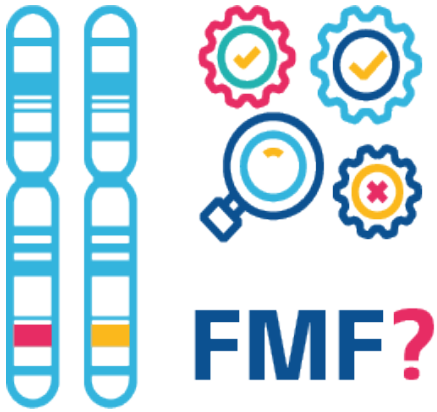
A new diagnostic test for FMF patients with unclear genetic profile

Source: Magnotti F. et al, Annals of the Rheumatic Diseases (09/10/20)

While the gene responsible for Familial Mediterranean Fever (FMF) disease is well known, the associated genetic testing sometimes leads to inconclusive result. Additional tools are required to avoid diagnostic wandering and delays in treatment initiation.

Unmet needs in the diagnosis of FMF patients

FMF is a hereditary autoinflammatory disease associated with recurrent fever and abdominal pain. FMF diagnosis is a two-step process: first based on clinical criteria, the diagnosis is confirmed by a genetic test that assesses the mutation profile of the *MEFV* gene. In most cases, both copies of the gene are mutated (bi-allelic mutations). Identifying two clearly pathogenic *MEFV* mutations is thus a reliable confirmation of a FMF diagnosis. Whereas, identifying only a single *MEFV* mutation (mono-allelic, nearly 1/3 of cases) or a *MEFV* mutation of unknown significance prevents confirmation.



Can we quickly identify FMF patients with unclear genetic profile?

A non-genetic diagnosis test for early prioritising and profiling of FMF patients

The *MEFV* gene encodes pyrin. Scientists discovered that a specific modification (called dephosphorylation) of pyrin leads to inflammasome activation in FMF patients but not in healthy controls. On that basis, they developed a fast and low-cost diagnostic test able to differentiate FMF patients (both bi- and mono-allelic) from healthy donors and from patients suffering from other inflammatory disorders. Briefly, a chemical (UCN-01) able to trigger dephosphorylation is applied on collected white blood cells of the patient and the test measures the subsequent kinetics of pyroptosis (a type of cell death) and the release of IL-1b (a marker of inflammation) afterwards. If both markers are high, the FMF diagnostic is confirmed.

Some work remains to be done to further demonstrate whether the test can 1) diagnose FMF patients with *MEFV* mutation of unknown significance and 2) be run on whole blood samples to allow for routine use in the clinics. Nevertheless, such a test would be of utmost importance to decrease the diagnostic uncertainty and guide early clinical decisions.

Patients and medical practitioners are gratefully acknowledged for their contribution to the work.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 779295