Genetic diversity: Crucial for our survival in many ways

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(Medical Xpress) -- Thanks to the sequencing of the 27 known human interferon genes, researchers from the Institut Pasteur and the CNRS reconstruct the genetic history of these proteins so central for our immune system, and put forward potentially innovative ways to improve the clinical use of interferons in the treatment of pathologies such as Hepatitis C, multiple sclerosis, and some cancers. These results are published on December 19th, 2011, in the *Journal of Experimental Medicine*.

Interferons are small proteins that allow the immune cells to communicate and, as such, play an important role in the stimulation of our natural defences. There are three different types of interferons that differ in their functions, but also in their genetic variability. The team led by Lluis Quintana-Murci, head of the Institut Pasteur/CNRS Unit of Human Evolutionary Genetics, focused on this last point and analyzed the genetic diversity of every interferon across various human populations.

“By using an evolutionary genetics approach, we were able to identify which interferons could be essential to our survival, and which ones could be less important or have a more redundant role,” explains Mr. Quintana-Murci. “We think that the interferons that are evolutionarily constrained have a more specific and important role in the fight against pathogens; as such they could represent more adapted therapeutic targets for future innovative and more efficient treatments.”

The various members of the type 1 interferon family (alpha/beta interferons), for example, show a very broad genetic variability. This result leads the researchers to consider that this family is very adaptable when exposed to a new pathogen, but also that some type 1 interferons have more essential roles than others.

On the contrary, the only type 2 interferon (gamma interferon) never shows any protein change from one individual to another. This high conservation testifies to its extremely specific and irreplaceable role in immune responses, in this case against mycobacteria.

As for the type 3 interferon family (lambda interferons): its genetic variability varies strongly depending on the geographical origin of the individuals. Their analyses showed that the European and Asian populations carry mutations that have conferred them, over time, a selective advantage to better adapt to their pathogenic environment, most probably reflecting an adaptation to viral pressures.

Globally these results argue in favour of a more targeted and precise medical use of interferons. The interferon alpha2, for example, is currently used in the treatment of chronic hepatitis C and of some cancers. However it may be relevant to use another type I interferon subtype that would have a more precise action with less side-effects.

More information: Evolutionary genetic dissection of human interferons, *Journal of Experimental Medicine*, en ligne le 12 Dec 2011, Jérémy Manry et al.

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