

A new approach for deciphering complex immune responses

The response to infection is highly variable from one individual to another. The Milieu Intérieur consortium, coordinated by Prof. Matthew Albert (Immunobiology of dendritic cells Unit, Institut Pasteur / Inserm) and Dr Lluís Quintana-Murci (Human Evolutionary Genetics Unit, Institut Pasteur / CNRS) seeks to establish the parameters that characterize the immune system of healthy individuals and its natural variability. In a study just published (August 25th) in *Cell Reports*, the researchers describe a new approach for analyzing the inflammatory response at the gene expression level in blood samples from healthy individuals, which reproduces the conditions of *in vivo* stimulation.

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The striking result from this study is that the immune response to complex stimuli such as bacteria, viruses, and fungi could be defined and distinguished based on a small number of genes that were induced by 4 key immune proteins or cytokines. In particular as few as forty-four genes, that were identified by machine learning techniques, could explain the variance present within such diverse immune responses.

In the era of high-throughput sequencing approaches which have huge challenges for data analysis and medical applications, this study suggests that simplified approaches if properly targeted may provide more effective solutions with easier clinical translation. In addition the study highlights that the utilization of highly standardized techniques for all steps including sample collection, sample preparation, and data analysis results in the generation of higher quality and more informative data.

In support of the published article, reference values are provided for each immune stimuli which reflects the natural variation of immune responses in humans. An online application was also released which provides an opportunity for the scientific community to exploit these data and to explore which genes are induced by a variety of immune stimuli.

This newly established approach is now being applied to the 1000 healthy donors within the Milieu Intérieur cohort, which will enable the dissection of how age, gender, environment, lifestyle, and genetics contribute to variable immune responses. This is a first necessary step on the path towards precision medicine approaches.

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Standardized whole-blood transcriptional profiling enables the deconvolution of complex induced immune responses, *Cell Report*, August 25, 2016

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