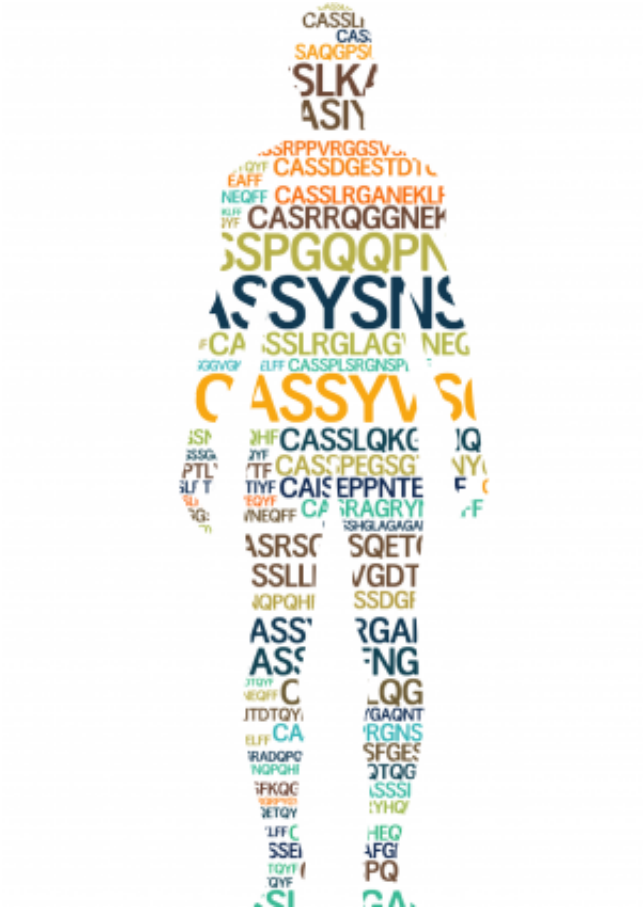
The language of T lymphocytes deciphered, the Rosetta Stone of the immune system

January 23 2015



How can our immune system defend us against aggressors so diverse such as viruses, parasites, fungi and tumours? The secret lies in the large number of clones of T and B lymphocytes, each of which expresses a

particular specific receptor. Until a few years ago, deciphering the complexity of this vast repertoire was considered impossible. A "Rosetta stone," or a key for decoding, was missing in order to "translate" and understand this "language" in all its complexity. Today, thanks to the development of new methods for DNA sequencing (Next Generation Sequencing, NGS), it is possible to obtain millions of sequences that represent the "identity card" of T lymphocytes. But how is it possible to use this data to trace back to the specificity of the single clones, and how can we understand their function?

The discovery

This question has now been answered by a study published on January 23rd in the prestigious journal *Science* and conducted by a group of researchers led by Federica Sallusto from the Institute for Research in Biomedicine of Bellinzona (Università della Svizzera italiana). The study describes a new approach that allows deciphering the language of T lymphocytes, which are cells of the immune system that protect us from pathogens and tumours. Combining methods of Next Generation Sequencing with in vitro stimulation and analysis of specific T cells, the researchers were able for the first time to establish a complete catalogue of the immune response to pathogens and vaccines. In particular, they have catalogued all the clones that respond to a particular microorganism, determining their specificity and their functional properties, for example their ability to produce inflammatory mediators (cytokines) or to migrate to different tissues.

The research results are surprising from many points of view. First, the repertoire of specific T lymphocytes is very broad and includes thousands of clones, each characterised by a different receptor. A second unexpected result is that, within the same clone, the cells can become specialised to perform different functions and to migrate to different tissues.

According to Federica Sallusto, "using this new approach we can rapidly decipher the language of T lymphocytes, that is, their identity, specificity and function, and we can do it for the thousands of clones that mediate the immune response against microbes and vaccines. In this way we discovered that when a naive T cell recognizes a pathogen and proliferates in order to eradicate it, the progeny cells may undergo different fates, such as acquiring the ability to produce different types of cytokines or to migrate to different tissues of the organism. This extreme flexibility of T lymphocytes represents a new element that explains how the human immune system is able to respond to attacks with different

weapons and on several fronts ."

More information: Becattini, S., D. Latorre, F. Mele, M. Foglierini, C. De Gregorio, A. Cassotta, B. Fernandez, S. Kelderman, T.N. Schumacher, D. Corti, A. Lanzavecchia, and F. Sallusto. 2014. "Functional heterogeneity of human memory CD4+ T cell clones primed by pathogens or vaccines." *Science*. 1260668. DOI: 10.1126/science.1260668.

Provided by Institute for Research in Biomedicine of Bellinzona