HLA genes and autoimmune diseases: the case of HLA-B27 alleles in Ankylosing Spondylitis

Mon, 25/06/2012 - 16:49 — admin

Gruppo di Ricerca:
Maria Teresa Fiorillo, Fabiana Paladini, Giorgio Camilli, Valentina Tedeschi, Carolina Vitulano, Sinem Tuncer, Silvana Caristi, Antonino Cassotta, Nicla Porciello and Rosa Sorrentino

Attach English:
Fiorillo.doc [1]

Major Histocompatibility Complex (HLA in humans) class I molecules are needed to trigger an effective cytotoxic immune response directed against microbial antigens. In some unlucky circumstances however, this response can be directed against endogenous proteins, thus leading to an autoimmune disorder. Ankylosing Spondylitis (AS) is a chronic inflammatory, autoimmune disease in which the 90-95% of patients carry the MHC class I allele HLA-B27, thus suggesting that these molecules are specifically involved in AS pathogenesis. However, although the intense investigation and the advent of new tools, the molecular mechanism underlying this association is not fully understood. We have identified in Sardinia one HLA-B27 allele, named B*2709, not present in patients and differing for a single amino acid (H116D) from the ancestral AS-associated B*2705. Many studies have been focused on this pair of alleles highlighting structural and functional features that might explain their different role in the disease pathogenesis. By means of crystallographic studies we have shown how some viral peptides can assume different conformations when bound to either allele, thus triggering a different CTL response. We have also identified some self peptides which drive a CTL response in the B*2705 patients but not in the B*2709 positive individuals. Our working hypothesis, supported by molecular dynamics studies, is that minor structural/functional differences contribute to an effective triggering of a cytotoxic response in patients and this is, at least partially, due to the nature of the amino acid at position 116. Work is in progress using ad hoc B27 mutants that should help to better define the structural as well as the consequent functional differences that the D116H polymorphism can produce.


Anno del Convegno:
2012

Source URL (retrieved on 11/10/2017 - 02:57): http://bbcd.bio.uniroma1.it/bbcd/en/node/5983

Links: