Retrovirology

Poster presentation

The switch from the standard proteasome to the immuno proteasome in the mononuclear cells of children with vertically acquired HCV infection

Alda Alfarano*, Antonella Versace, Gabriellla Bertolotto, Simona Vatrano and Pier-Angelo Tovo

Address: Departement of Paediatrics, University of Turin, Turin, Italy
* Corresponding author

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Background

The mechanisms responsible for the HCV escape to the immune system remain largely unknown. A strict interaction between NS3, a non-structural protein of HCV, and the LMP-7, a subunit of the immunoproteasome, has been described suggesting that this may result in an impaired antigen presentation. Proteasomes are intracellular multicatalytic complexes whose primary function is the degradation of abnormal or foreign proteins. In particular, they regulate the presentation of viral antigens onto MHC I molecules. The 26S proteasome has a 20S catalytic core and two 19S regulatory complexes. Three subunits (β1, β2 and β5) are responsible for the main proteasomal peptidase activities (PGPH, trypsin-like, and chymotrypsin-like activity, respectively). With certain cytokines, such as interferon-γ (IFN-γ), the three β subunits of the standard proteasome (PS) are replaced by inducible subunits (LMP-2, MECL-1 and LMP-7) to form the immunoproteasome (IP), which improves the antigen processing and presentation.

Materials and methods

Total RNA was extracted from PBMCs of 13 HCV infected children and 50 healthy controls. 1μg RNA was reverse-transcribed and a real-time quantitative PCR was used to evaluate the expression of standard proteasome genes (β1, β2 and β5) and of immunoproteasome genes (LMP-2, MECL-1 and LMP-7). The values obtained were normalised using Abelson as the control gene and the results were expressed using the DDCT method. The results were compared by Wilcoxon's test.

Results

In the control group the median expressions of PS genes were: β1=1.75 (range 0.70-2.80), β2=1.29 (range 0.67-1.91) and β5=1.08 (range 0.63-1.54); the median expressions of IP genes were: LMP-2 =1.79 (range 0.59-3.0), MECL-1=1.58 (range 0.58-2.58) and LMP-7=1.32 (range 0.48-2.17); the median value of a subunits was 1.04 (range 0.37-1.72). In HCV infected children the median expressions of PS genes were: β1=0.52 (range 0.17-1.19), β2=1 (range 0.44-3.52) and β5=0.48 (range 0.49-1.53) and those of IP genes: LMP-2=1.56 (range 0.27-2.43), MECL-1=1.33 (range 0.14-2.14) and LMP-7=1.53 (range 0.25-1.40). The difference was significantly higher for LMP-7 expression in HCV infected children.

Conclusions

There is a significant higher expression of IP genes in HCV infected children. This switch from PS to IP presumably reflects an adaptive response aimed at increasing antigen presentation and T cell reactivity. However, the interaction of NS3 protein with LMP-7 might frustrate this effort allowing the virus to escape. Conversely, the switch from PS to IP may lead to an increased presentation of self-antigens onto MCH I molecules, ultimately resulting in enhanced autoimmune responses.