Asymptomatic long term non-progression

PE22

Characterization of anti-gp41 antibodies eliciting viral neutralization and protecting against CD4 depletion in long-term non-progressors

Vieillard V.[1], Samri A.[1], Lucar O.[1,2], Crouzet J.[2], Costagliola D.[3], Debré P.[1], French ALT Study Group
[1]CIMI-Paris, INSERM U 1135, Paris, France, [2]InnaVirVax, Evry, France, [3]Institut Pierre Louis d'Epidémiologie et de Santé Publique, Paris, France

Background: We previously showed that antibodies (Ab), which recognized a highly conserved motif of the gp41, called 3S, are protective against CD4+ T cell depletion. This was analyzed after immunization in a model of SHIV162P3-infected macaques, and naturally in asymptomatic long-term non-progressor (ALT) patients. More recently, we have detected the presence of anti-3S/W614A Ab, which recognized a point-modified form of 3S, in less than 5% of HIV-1 progressor patients. These Ab remain able to protect CD4+ T cells but have also acquired the capacity to elicit viral neutralization. Here, we quantified and characterized these anti-3S W614A Ab in non-treated patients from the French ANRS ALT cohort.

Methods: 64 HIV-1 untreated ALT patients who had enrolled with >600 CD4+ cells /mm3 (for at least 8 years), were followed-up each year during the first 3 years to evaluate anti-3S-W614A Ab. Ab level was measured by ELISA, and its presence was correlated with different biological parameters (CD4 count, CD4/CD8 ratio, viral DNA, viral load, …). Viral neutralization was performed against a panel of tiers 1 and 2 viruses, using the standard TzM-bl assay.

Results: 25.7 % of patients had detectable anti-3S/W614A Ab at the enrollment period. The presence of these Ab is highly significantly correlated with an increased of the CD4/CD8 T cell ratio ($p=0.006$), and both decreased of the viral load ($p< 0.0001$) and viral DNA ($p=0.0003$). In the same subjects, measured again at 24-36 months following inclusion in the cohort, we observed that subjects with persistently specific Ab still had both significantly lower viral DNA and viral load, as compared to patients without anti-3S/W614A Ab. Importantly; we also report that the efficacy of viral neutralization mediated by anti-3S/W614A Ab, is time-dependent, increasing during the follow-up in term of breadth and potency.

Conclusions: The presence of anti-3S W614A Ab appears to confer crucial advantage in asymptomatic long-term non-progressor HIV-1 patients. These results bring new insights for both pathophysiological research and development of new vaccine strategy.