

**SEMINAIRE**

***IPBS , salle de conférence n° 1 , niveau 2  
205 route de Narbonne TOULOUSE CEDEX 4***

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**Lundi 15 octobre 2007 à 11 h.**

**Dr Loïc DUPRE** (U563, INSERM Toulouse)

***" Multiple T lymphocyte defects in The Wiskott-Aldrich syndrome "***

The Wiskott-Aldrich syndrome (WAS) is a severe immune deficiency characterized by susceptibility to infections, bleeding disorders, auto-immunity and cancer. WAS is due to mutations in the gene encoding the WAS protein (WASP), which controls Arp2/3-dependent actin nucleation in hematopoietic cells following activation through numerous membrane receptors. We have characterized the specific role of WASP in individual T cell subsets, by comparison of cells isolated from WAS patients and healthy donors.

In CD4<sup>+</sup> T helper cells, WASP participates to immunological synapse assembly and stability, therefore setting the threshold for TCR-driven activation. In these cells WASP deficiency results in reduced transcriptional activation of Th1 type cytokines. In CD4<sup>+</sup>CD25<sup>+</sup>Foxp3<sup>+</sup> T regulatory cells, WASP appears to also contribute to TCR-driven activation and is required for normal suppressive activity. Finally in CD8<sup>+</sup> cytotoxic T cells, TCR-driven proliferation and cytokine production are profoundly impaired, while cytotoxic activity appears to be preserved. These data suggest that several components of T cell immunity are compromised in WAS patients and could underline defects in tolerance and response to pathogens and tumors.

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