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Pro-inflammatory roles of the death receptor-CD95

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CD95 (also known as Fas) is a death receptor that belongs to the TNF receptor superfamily and plays a pivotal role in immune surveillance. Upon binding of its cognate ligand CD95L, the intracellular region of CD95 recruits the adaptor protein FADD, which in turn binds caspases -8/-10. This complex called DISC, for Death Inducing Signalling Complex allows caspase clustering, which is instrumental in their activation and the subsequent induction of apoptosis.

CD95L is detected mainly at the surface of innate and adaptive immune cells where it contributes to the elimination of infected and transformed cells. We recently found that the amount of CD95L is increased in sera of patients affected by chronic inflammatory disorders as compared to healthy subjects and correlates with disease progression. Although this soluble form of CD95L arises from the cleavage by metalloproteinases of the cytotoxic transmembrane ligand, it fails to kill cells. Instead, it promotes accumulation of activated T-cells in inflamed organs through the induction of a "non-orthodox" Ca2+/PI3K signaling pathway that relies on the implementation of a new CD95-containing complex that we designated MISC for Motility-Inducing Signalling Complex (Tauzin et al., PLoS Biol, 2011).

These findings emphasize that according to its stoichiometry, CD95L does not only behave as a pro-apoptotic cytokine but can also implement non-apoptotic signaling pathways promoting cell migration. These results will open new avenues into the study of the death receptor signaling and provide insight into its role in carcinogenesis.

Biography

Legembre has completed his PhD from University of Bordeaux-2 (France) and postdoctoral studies from University of Chicago (USA). He is currently Team leader in IRSET, University of Rennes-1. He has published more than 29 papers in peer-reviewed journals and serving as editorial board member and as associate editor for Recent Patents on Anti-Cancer Drug Discovery.

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