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REGULATION OF THE CATALYTIC ACTIVITY OF THE HUMAN PHOSPHATASE PTPN4 AND ITS INTERACTION WITH THE MAPK P38γ

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The human PTPN4 belongs to the protein tyrosine phosphatase (PTP) family. PTPN4 contains an N-terminal FERM, a central PDZ domain and a C-terminal PTP domain. PTPN4 protects cells against apoptosis and targeting its PDZ domain abrogates this protection .We documented the regulatory mechanisms of PTPN4 and showed that the PDZ domain inhibits the phosphatase activity of PTPN4 and that the mere binding of a PDZ ligand is sufficient by itself to release catalytic inhibition. The PDZ-PTP supramodule adopts a compact conformation in solution and the PDZ ligand disrupts transient inter-domain communication, thereby allosterically restoring the catalytic competence of PTPN4. The inter-domain linker is mandatory to this regulation of PTPN4 catalytic activity. We have recently identified that PTPN4 interacts with the MAP kinase p38γ. The C-terminus of p38γ (p38γ-Cter) targets the PDZ domain of PTPN4, promoting massive cell death of human glioblastoma upon intracellular delivery. We identified the molecular basis of the recognition of p38γ-Cter that displays the highest affinity among all endogenous partners of PTPN4 and we reported the molecular interactions *in vitro* between the full-length kinase and the phosphatase PTPN4.

Biography

Celia Caillet-Saguy studied Biochemistry and obtained her PhD at Paris Diderot University (Paris7). Her thesis made in the NMR unit at the Institut Pasteur focused on the study of heme acquisition mechanism in bacteria. She used biophysical approaches, mainly nuclear magnetic resonance. She joined the team of Biocrystallography led by Stéphane Bressanelli in the Molecular and Structural Virology Unit (France) for a 3-year Postdoc. Her project focused on the study of genome replication of hepatitis C virus. She acquired a dual expertise in NMR and X-ray crystallography. Then she joined the team of Nicolas Wolff at the Institut Pasteur. She is interested in disturbance by viruses of the signalling pathways of the infected cell involving PDZ domains. In 2014, she became an Assistant Professor. Her work has resulted in 14 peer-reviewed publications and 12 presentations as speaker in conferences. Her publication H-index is 10.

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