Seminar/Talk

"Reengineering CRISPR-Cas effectors"

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Host: Prof. Jack Bravo

CRISPRCas9s clinical utility is constrained by strict PAM requirements and the inability to package large nucleases into AAV vectors. We engineered a modular Cas9, split into a nuclease scaffold and an exchangeable PAM-interacting domain (PID). This architecture enables one scaffold to function with multiple PIDs, allowing ultra-multiplexing and simple PID swapping to target all disease-relevant loci. Guided by cryo-EM, we identified functional split sites, validated activity with a GFP reporter assay, and restored fast cleavage kinetics using intein-mediated ligation. Exchanging PIDs broadened PAM compatibility significantly, with several split chimeras achieving robust editing across any site in human cells. This precision nuclease system offers a compact, PAM-flexible platform that fits within a single AAV and establishes a path toward versatile, clinical genome-editing therapies.

Wednesday, April 1, 2026 03:00pm - 04:30pm
Central Bldg / O1 / Mondi 2a (I01.O1.008)

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