From Structural Dynamics to Spatial Omics: a dual strategy against arboviruses

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Arboviruses represent an escalating global health emergency, amplified by climate change, rapid urbanization, and expanding vector habitats. Developing effective preventive and therapeutic countermeasures requires deep insights into viral structural biology, pathogenesis, and host interactions. At Area Science Park, our Virology Unit addresses this challenge through a dual approach: rational, structure-guided antigen design and high-throughput profiling of host-pathogen interfaces.

Our first research line tackles a central bottleneck in flavivirus vaccine design: balancing potent neutralization against the risk of cross-reactive antibodies that drive Antibody-Dependent Enhancement (ADE). A factor involved in this antigenicity is "viral breathing," the dynamic structural fluctuation of the Envelope (E) protein. In a case study comparing two closed Zika virus strains (PE243 vs. PRVABC59), we showed that PE243 displays attenuated pathogenicity, restricted dissemination, and reduces susceptibility to polyclonal neutralization despite identical in vitro replication. To complement these findings, molecular dynamics simulations were applied to investigate E protein flexibility in the context of the full virion. Mapping these structural determinants may allow the design of more stable immunogens that elicit broad protection without ADE.

Our second research line disentangles virus-host interactions by mapping how infection alters intracellular architecture. Viruses routinely reorganize organellar protein and RNA composition to drive replication, hijack translation, and evade antiviral defenses. Our ORCHESTRA platform aims to established a BSL-3-compatible organelle isolation pipeline for high-throughput multi-omics. This framework enables systematic spatial profiling across membrane-bound and membrane-less organelles, uncovering novel antiviral targets.

Short bio: Giuditta De Lorenzo is the Head of the Virology Unit at Area Science Park. Her research integrates molecular virology, virus-host interactions, structural vaccinology.
She developed her scientific career at the MRC-University of Glasgow Centre for Virus Research (CVR) by developing flavivirus vaccine candidates, isolating

monoclonal antibodies, and uncovering crucial biological aspects of emerging SARS-CoV-2 variants within the national G2P-UK consortium.
At Area Science Park, she is working in close interaction with the Laboratory of Data Engineering (LADE) to establishing an interdisciplinary research programme that combines experimental virology with advanced computational approaches.