PANDORA - Pandemics Outbreaks Rationalized: towards a universal therapy to eliminate intracellular pathogens and drug resistance

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Prof. Rizzello proposes here a research vision that aims to revolutionise the way we cure infections caused by intracellular pathogens, with the aim to find a universal therapy to infectious diseases that will also counteract the development of drug resistance.
In PANDORA, he will specifically focus on eradicating human tuberculosis, one of the worst pandemics so far.

To do this, he will first probe what are the molecular 'bar-codes' of infected cells, namely those specific membrane proteins that cells express upon infection.
He will use this to reversely engineer a repertoire of super-selective polymeric nanoparticles - known as Polymersomes - that will carry ligands to recognise, bind, and selectively attack infected cells only, while leaving non-infected cells completely untouched. Such nanocarriers will access the infected cells and locally deliver their payload, which is the core technology of the therapy. Such technology will be inspired by what nature invented: he will reproduce the binding sequence of autolisins, proteins expressed by bacteriophages that specifically bind the wall of Mycobacteria species (the agent causing tuberculosis).

He will thus create fusion antibodies (Ab) characterized by (i) the binding sequence of mycobacteriophages autolisins (for selective recognising intracellular Mycobacterial wall) and (ii) an effector region promoting bacterial clearance through either the macrophage-triggered phagocytosis or an ubiquitin-proteasome system.

This therapy will represent a complete revolution in the field of new antimicrobial development, as it will combine complete bacterial eradication, development of memory immunity and fight against drug resistance, the three core pillars of this project.
The super-selective polymersomes carrying the Abs-based universal therapy will be combined with the development of chimeric antigen receptor T-cells (CAR-T) against infection. These T-cells will be designed to chase and eradicate circulating infected cells in model organism.

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