Università degli Studi di Pavia

Dipartimento di Biologia e Biotecnologie
"Lazzaro Spallanzani"

Via Ferrata 9 - 27100 Pavia, Italia

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AULA BUZZATI-TRAVERSO

ORE 16:30

SEMINARIO

" Discovering and targeting *Bacillus anthracis*' Achilles heel: the new way to fight and cure Anthrax"

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Anthrax is a highly resilient and deadly disease caused by the spore-forming bacterial pathogen Bacillus anthracis. Today, anthrax mostly affects wildlife and livestock, but remains a concern for human public health primarily in persons handling contaminated animal products and as a bioterror threat due to the high resilience of spores, the high case-fatality rate even with the aggressive use of antibiotics and the lack of a civilian vaccine program. As part of its immune evasion strategy, the bacterium presents a dynamic cellular surface with a complex composition. In its vegetative form, the cell surface of B. anthracis is covered by one of two protective protein arrays known as the Sap or EA1 S-layer (surface layer), present during exponential and stationary growth phase, respectively.

The self-assembling characteristic of these S-layer proteins has thus far hampered their detailed structural and biophysical characterization. Successfully, Dr. Fioravanti applied Nanobodies (Nbs) as a bio-tool to control Sap polymerization and to accomplish its crystallization and structure determination, unveiling a new class of S-layer proteins with a novel mechanism of assembly independent of calcium. Amongst the isolated Nbs she was also able to identify Sap inhibitory nanobodies that prevented Sap assembly and depolymerized existing Sap S-layers in vitro. When applied in vivo, nanobody-mediated effacement of the Sap S-layer resulted in severe morphological defects and proved bacteriostatic unlike the genetic knockout of sap.

Encouraged by these findings, anti-Sap S-layer inhibitors are being developed as new promising tools to fight anthrax disease. To date, this novel anti S-layer Nanobody therapy resulted in clearance of ongoing B. anthracis infection in a mouse model curing them of lethal anthrax. These findings expose, for the first time ever, disruption of S-layer integrity as a mechanism with therapeutic potential in S-layer carrying pathogens.

Su invito della prof. A. Albertini