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T cell clones and somatic mutations in refractory celiac disease

Mercoledì 02 Luglio
ore 15.00 - 16.00

Aula Magna Mangiagalli
via della Commenda, 12

Summary

Autoimmune diseases remain among the most challenging conditions to treat due to their heterogeneity, lack of precision therapies, and significant off-target effects from existing immunosuppressive drugs.
Refractory coeliac disease (RCD) and enteropathy-associated T-cell lymphoma (EATL) are rare, severe autoimmune disorders with no effective targeted therapies.
This project introduces AI-BODY, a modular discovery platform that combines single-cell multi-omics with cuttingedge AI models to identify disease-driving lymphocytes and design bispecific antibodies (BsAbs) that selectively eliminate them.
AI-BODY integrates structural prediction tools, antibody design engines, and developability screening to generate optimised BsAb candidates.
We hypothesise that low-affinity BsAbs targeting co-expressed antigens (e.g., CD58, CD49b, CD244) will offer high specificity for pathogenic intraepithelial lymphocytes (IELs), while sparing healthy cells.

The project comprises:
1. Identification of aberrant immune cell subsets via single-cell transcriptomics and surface proteomics;
2. AI-guided design and affinity tuning of BsAb constructs;
3. Functional validation using ADCC and binding assays in patient-derived IELs.
Our interdisciplinary team—spanning immunology, AI/ML, antibody engineering, and clinical gastroenterology—has access to rare patient samples, established protocols, and preliminary data supporting feasibility.
The AI-BODY platform is designed to be scalable and adaptable to other autoimmune diseases and cancers, offering a transformative path toward precision immunotherapy.

We propose to develop a new treatment for a serious gut condition called refractory coeliac disease and a related cancer. Using artificial intelligence and advanced genetic tools, we will create precise antibodies that detect and eliminate harmful immune cells driving the disease. This innovative strategy could lead to safer, more effective therapies for people with autoimmune conditions and related cancers, where current treatments are often limited or
cause severe side effects.