Project Summary
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Exploiting newly identified anti-tumor TCRs to dissect the T cells/leukemia interplay in acute myeloid leukemia

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Dressing T lymphocytes with T cell receptors (TCRs) specific for relevant tumor antigens generates living drugs, able to kill the tumor, persist long term and patrol for tumor relapse. Still, pinpointing the most clinically relevant cancer-specific TCR remains a major bottleneck. In fact, despite the huge efforts required to identify promising novel receptors, the anti-tumor efficacy of the engineered T cell products remains a major issue and the observed clinical responses are often disappointing. Starting from specimens retrieved from patients affected by acute myeloid leukemia, we will combine single cell omics, state-of-the art T cell engineering and functional validation of the lymphocytes to correlate the immunological signature of cancer-specific T cells with the potency of the anti-tumor TCRs, and to comprehensively unravel the complex evolution occurring in AML when different immunological pressures are applied. The overall aim is to provide key hints for streamlining the discovery of clinically relevant TCRs and for proposing novel targeted and combined therapeutic strategies able to (re)instate tumor immunosurveillance and patrol for cancer relapse.