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DBS SEMINAR

Tuesday, December 19th, 2023 – 12h15
Zoom Meeting and Seminar room 06, Bugnon 7

"Deconstructing aging with senolytic CAR T cells."

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Host: Prof. Alejandro Ocampo

Abstract

Prophylactic and long-lasting therapeutic efficacy of senolytic CAR T cells against age-related phenotypes

Senescent cells accumulate in organisms over their lifespan and play a key role in age-related tissue decline and the development of chronic aging pathologies. Thus, effective strategies to eliminate senescent cells (senolytics) could have broad therapeutic implications. In a departure from conventional chemical approaches we developed the first cell-based senolytic therapy based on chimeric antigen receptor (CAR) T cells targeting uPAR, a cell-surface protein upregulated on senescent cells. Our initial proof of concept showed their efficiency in young animal models of liver fibrosis and cancer. We now show that uPAR-positive senescent cells accumulate during physiological aging and characterize their cell types and expression profiles. Importantly, we find that they can be safely targeted with senolytic CAR T cells in aged animals where they result in significant improvements in both tissue regeneration and metabolic function. Of note, we find that the beneficial effects of senolytic CAR T cells are long lasting; single administration of a low dose is sufficient to safely achieve long-term therapeutic and preventive effects in healthspan.

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