Local immune checkpoint inhibition

Reference No: B75080

CHALLENGE

Antibodies targeting immune checkpoint molecules offer promising tools in cancer immunotherapy. However, drawbacks of this approach are systemic side effects since immune checkpoint molecules are expressed both on healthy and tumor cells.

INNOVATION

Here novel trispecific molecules **(LiCADs, local inhibitor checkpoint antibody derivatives)** comprising **binding sites** with specificity for a **tumor cell,** for an **effector cell** and for a **checkpoint molecule,** respectively, are presented. In this construct the affinity of the checkpoint molecule binding site is rather weak especially compared to the tumor targeting binding site. Thus **checkpoint binding is restricted and concentrated to tumor cells** avoiding undesired toxicity to healthy cells and accordingly systemic side effects.

LiCAD molecules consisting of:

- the **endogenous SIRPα domainto block the CD47**- SIRPα signaling pathway
- a single chain variable fragment (scFv) **binding to a tumor antigen**
- a scFv to trigger **recruitment and activation of effector cells**

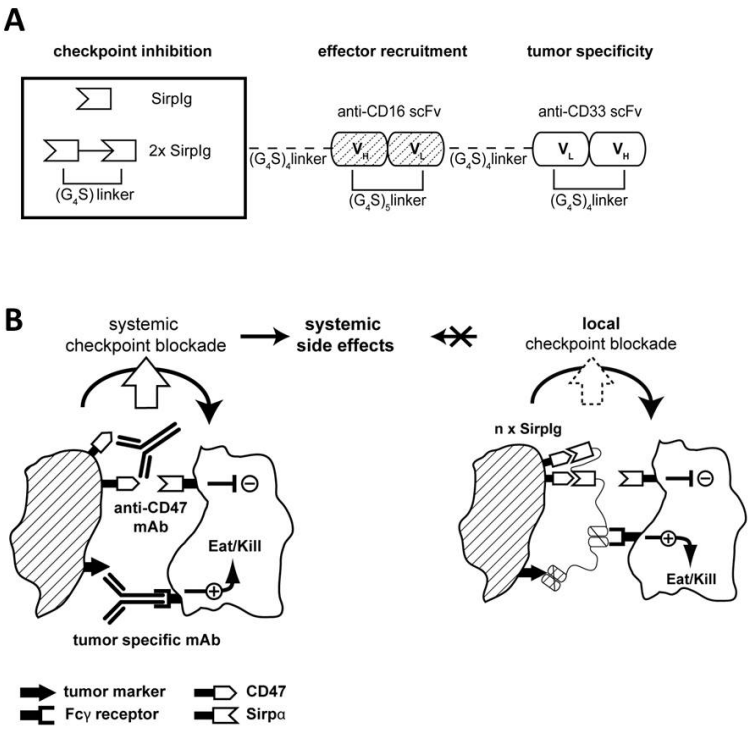

Figure A: Structure of LiCADs; **Figure B:** conventional treatment (left) vs LiCAD treatment (right)

COMMERCIAL OPPORTUNITIES

- Local (tumor) immune checkpoint inhibition avoiding systemic side effects
- Exchangeable modules (binding elements) adaptable for specific tumor and/or effector cells

DEVELOPMENT STATUS

- In vitro experiments with different tumor cell lines and with primary AML patient cells have successfully been performed
- Module optimization

REFERENCE:

Ponce et al., Oncotarget, 2017;8 (7), 11284-11301

IP rights:
PCT filed in 2016

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