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There are roughly 17 tumor-targeting therapeutic monoclonal antibodies (mAbs) currently approved for oncological indications. These antibodies can mediate their effects through a number of mechanisms including blockade of survival signals, programmed cell death induction, complement-dependent cytotoxicity, FcγR-mediated antibody-dependent cell cytotoxicity, and phagocytosis of mAb-opsonized target cells. FcγR-mediated mechanisms must be considered in the context of the innate and adaptive cells that express them: mast cells, basophils, eosinophils, monocytes, macrophages, neutrophils, natural killer cells, B cells, and dendritic cells. For example, Fc mutations favoring expression of FcγRIIa on dendritic cells have been described to lead to T cell memory against the target of the antibody. Such a memory response or “vaccinal effect” to CD20 has been suggested in some patients treated with Rituximab, an anti-CD20 IgG1 antibody. Similar mechanisms could be employed to improve next-generation biologics by harnessing Fc receptors that mediate favorable biology. Despite significant advances in this field, understanding the molecular underpinnings driving immune cell recruitment and function in the tumor microenvironment remains elusive. One challenge is that FcγR biology is poorly modeled in vivo because murine FcRs do not faithfully recapitulate human FcR expression or because FcγR activity can be impaired in immunocompromised mouse models. We aim to combine antibody engineering technology with appropriate in vitro mechanistic experiments that utilize human immune cells, and ultimately with engineered models to dissect the mediators of FcγR function to better understand the interplay among therapeutic antibodies, tumors, and the immune system.

## Selected Publications

A novel antibody-drug conjugate targeting SAIL for the treatment of hematologic malignancies.
Kim SY, Theunissen JW, Balibalos J, Liao-Chan S, Babcock MC, Wong T, Cairns B, Gonzalez D, van der Horst EH, Perez M, Levashova Z, Chinn L, D'Alessio JA, Flory M, Bermudez A, Jackson DY, Ha E, Monteon J, Bruhns MF, Chen G, Migone TS.

*Blood Cancer J. 2015 May 29;5:e316.*

Quantitative assessment of antibody internalization with novel monoclonal antibodies against Alexa fluorophores.
Liao-Chan S, Daine-Matsuoka B, Heald N, Wong T, Lin T, Cai AG, Lai M, D'Alessio JA, Theunissen JW.
*PLoS One. 2015 Apr 20;10(4):e0124708.*

Core promoter recognition complex changes accompany liver development.
D'Alessio JA, Ng R, Willenbring H, Tjian R.
*Proc. Natl. Acad. Sci. USA. 2011 Mar 8;108(10):3906-11.*

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