Peptide Therapeutics for Tissue Regeneration

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The talk will describe the development of peptide agonists for selective and precise activation of signaling transduction cascades invovled in cellular reprogramming and tissue regeneration. In particular, we built a peptide drug discovery platform for the identification of *de novo* binders to drug targets of therapeutic relevance. We discovered disulfide-constrained peptides that promote Wnt signaling activity by modulating the cell surface levels of ZNRF3, an E3 ubiquitin ligase that controls the abundance of the Wnt receptor complex at the plasma membrane. Our work highlights a strategy for the development of potent, biologically active peptide agonists via targeting cell surface receptor complexes and signaling.

Selected publications:

[1] Kschonsak YT, Gao X, Miller SE, Hwang S, Marei H, Wu P, Li Y, Ruiz K, Dorighi K, Holokai L, Perampalam P, Tsai WK, Kee YS, Agard NJ, Harris SF, Hannoush RN*, de Sousa E Melo F*. *Cell Chem. Biol.* **2024**, 31(6):1176-1187.e10.

[2] Li Y, Wei Y, Ultsch M, Li W, Tang W, Tombling B, Gao X, Dimitrova Y, Gampe C, Fuhrmann J, Zhang Y, Hannoush RN*, Kirchhofer D*. *Nat Commun.* **2024**, 15(1):4359.

[3] Gao X, Kaluarachchi H, Zhang Y, Hwang S, Hannoush RN*. *PLoS One.* **2024**,19(3):e0299804.

[4] Yun J, Hansen S, Morris O, Madden DT, Libeu CP, Kumar AJ, Wehrfritz C, Nile AH, Zhang Y, Zhou L, Liang Y, Modrusan Z, Chen MB, Overall CC, Garfield D, Campisi J, Schilling B, Hannoush RN*, Jasper H*. *Nat Commun.* **2023**, 14(1):156.

[5]Thakur AK, Miller SE, Liau NPD, Hwang S, Hansen S, de Sousa E Melo F, Sudhamsu J, Hannoush RN*. *ACS Chem Biol.* **2023**,18(4):772-784.

[6] Hansen S, Zhang Y, Hwang S, Nabhan A, Li W, Fuhrmann J, Kschonsak Y, Zhou L, Nile AH, Gao X, Piskol R, de Sousa E Melo F, de Sauvage FJ, Hannoush RN*. *PNAS* **2022**, *119(46):e2207327119.*