New drug development

78P DRUGGING THE UNDRUGGABLES - CELL-PERMEABLE PEPTIDE INHIBITORS OF THE WNT SIGNALING PATHWAY IN BREAST CANCER

V. Arndt, A. Friebe, K. Ross, F. Agerer, D. Friedrich, J. Waak, H. Hennemann, J. Vollmer
Late Discovery, Nexigen GmbH, Cologne, GERMANY

Dysregulation of Wnt signaling has been linked to a wide range of human cancers. Oncogenic activation of the Wnt pathway in breast cancer is particularly associated with aggressive tumor subtypes, including triple-negative breast tumors, and has been shown to play a critical role in the epithelial-mesenchymal transition of cancer cells, the regulation of cancer stem cells, and the development of chemoresistance. Due to the persistent dependence on Wnt signaling for tumor growth and survival, targeting the Wnt pathway represents a promising approach for breast cancer therapy.

Unfortunately, the development of pharmacological inhibitors has so far proved elusive, owing to the lack of druggable targets in the Wnt pathway. Nexigen aims to identify peptide drugs for such targets that can hardly be accessed by conventional small molecule drugs or therapeutic antibodies. Using our proprietary next generation peptide screening platform, we were able to identify cell-permeable peptides that effectively inhibit Wnt signaling in breast cancer cells in vitro and in vivo. Functional analysis of our most advanced peptide candidate demonstrates strong inhibition of cell migration, invasion, proliferation, and colony formation in different cancer cell lines, including triple-negative MDA-MB-231 breast cancer cells. Most importantly, we observed a significant suppression of tumor growth and ex vivo tumor cell colony formation in a xenograft triple-negative breast cancer model upon systemic drug exposure. Overall, our data suggest that our Wnt pathway peptide inhibitor could be a promising new drug candidate to be interrogated in a broad diversity of Wnt-dependent breast tumors.

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