

DR. KAY-UWE WAGNER (2015)

Identification of Candidate Target Genes for Metastasis and Cancer Cell Dormancy in a Novel Triple-Negative Breast Cancer Model

Lay Description of Outcomes: Using genome-wide gene expression analyses (RNA Sequencing) on paired tissue samples of primary and metastatic mammary tumors in novel triple-negative breast cancer models, the collective results obtained from this project established that molecular pathways controlling Integrin cell surface interactions and adhesion molecules may play a role in the metastatic progression. More importantly, metastatic cancer cells exhibited a significantly deregulated expression of numerous genes that have pivotal roles in the JAK/STAT signaling cascade that mediates the intracellular action of inflammatory cytokines. Experimental evidence was provided that the Janus kinase 1 (JAK1), and not JAK2 as commonly believed, is the key signaling node for the inflammatory cytokine-mediated activation of oncogenic STAT3 and metastatic progression. The outcomes of our studies have provided a solid scientific rationale for testing JAK1 tyrosine kinase inhibitors in preclinical models for cancer therapy to prevent the metastatic dissemination of malignant cells (i.e., from primary or secondary sites).

Related publication: Wehde, B.L.; P.D. Rädler; H. Shrestha; S.J. Johnson; A.A. Triplett and K.-U. Wagner (2018) Janus kinase 1 plays a critical role in mammary cancer progression. *Cell Rep.* 25: 2192–2207