

6TH WORLD FORUM ON BREAST AND CERVICAL CANCER



Thaís Dolzany de Oliveira¹, Alexander vom Stein¹, Rocio Rebolledo-Rios¹, Liudmila Lobastova¹, Marcus Lettau², Sabine Barnert³, Ottmar Janssen², Prerana Wagle⁴, Phuong-Hien Nguyen¹, Michael Hallek¹ and **Hinrich P. Hansen^{1*}**

¹University of Cologne, Department I of Internal Medicine, Center for Integrated Oncology Aachen Bonn Cologne Duesseldorf; Center for Molecular Medicine Cologne; Center of Excellence on Cellular Stress Responses in Aging-Associated Diseases, 50931 Cologne, Germany

Stromal cells support the survival of human primary tumor cells through Lyn-driven extracellular vesicles

Keywords

Extracellular vesicle, Lyn kinase, extracellular matrix, endosialin

Stromal cells and in particular cancer-associated fibroblasts (CAFs) support tumor cells and cause therapeutic resistance of many malignant diseases, including breast cancer. CAFs promote tumor cell growth through direct cell contact, soluble factors and extracellular vesicles (EVs). The protein tyrosine kinase Lyn is expressed in the malignant and stromal cells of breast cancer tissue. It serves as a significant prognostic factor of the disease and is associated with the triple-negative phenotype. We studied the role of Lyn in the EV-based communication between stromal and tumor cells. We compared the Lyn-dependent EV release, uptake and functionality using Lyn-proficient and -deficient stromal cells and primary CLL cells. Lyn-proficient cells caused a significantly higher EV release and EV uptake as compared to Lyn-deficient cells and also conferred stronger support of tumor CLL cells. Proteomic comparison of the EVs from Lyn-proficient and -deficient stromal cells revealed 70 significantly differentially expressed proteins. Gene ontology studies categorized many of which to organization of the extracellular matrix, such as collagen, fibronectin, fibrillin, Lysyl oxidase like 2, integrins and endosialin (CD248). In terms of function, a knockdown of CD248 in Lyn⁺ HS-5 cells resulted in a diminished B-CLL cells feeding capacity compared to wildtype or scrambled control cells. CD248 is a marker of certain tumors and cancer-associated fibroblast (CAF) and crosslinks fibronectin and collagen in a membrane-associated context.

Our data provide preclinical evidence, that the tyrosine kinase Lyn crucially influences the EV-based communication between stromal and primary tumor cells by raising EV release and altering the concentration of functional molecules of the extracellular matrix. (256).

6TH WORLD FORUM ON BREAST AND CERVICAL CANCER

Biography

Dr. Hinrich Hansen is a Professor in the Department of Internal Medicine I at the University Clinic Cologne, Cologne, Germany. His research expertise spans Clinical Pathology, Histopathology, Hematopathology, Surgical Pathology, and Diagnostic Pathology. Dr. Hansen has made significant contributions to the field through his extensive research and publications in leading international journals. He also serves as an editorial board member and reviewer for several reputed scientific journals. In addition to his academic and research accomplishments, he has successfully undertaken various administrative and leadership responsibilities. Dr. Hansen has authored numerous research articles and books focusing on Clinical and Experimental Pathology.