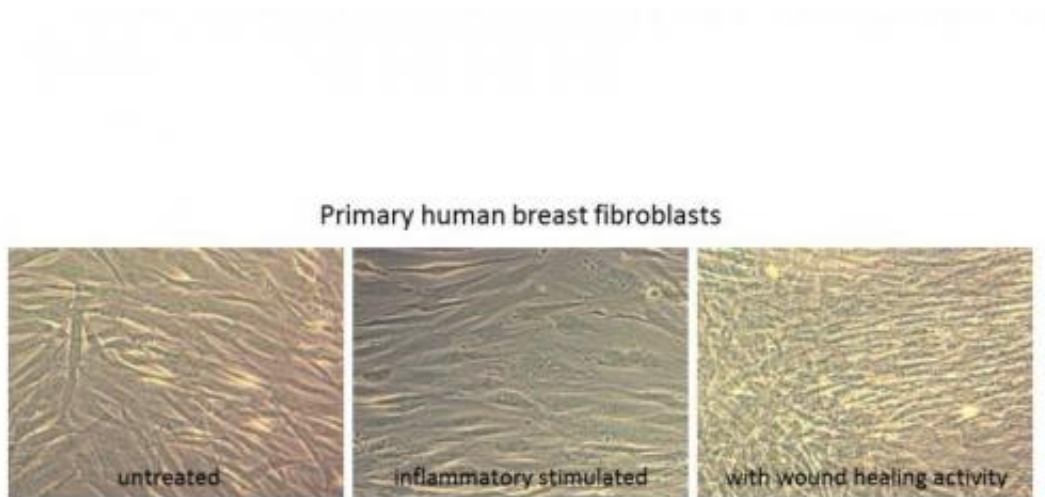


New analysis methodology may revolutionize breast cancer therapy

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Left hand side: untreated fibroblasts. Center: inflammatory stimulation hardly affects cell morphology. Right hand side: stimulation of wound healing activity results in proliferation and higher cell density. Credit: University of Vienna

Stroma cells are derived from connective tissue and may critically influence tumour growth. This knowledge is not new. However, bioanalyst Christopher Gerner and an interdisciplinary team from the

University of Vienna and the Medical University of Vienna have developed a novel methodology for investigation. Using modern mass spectrometry, tumour-promoting activities from breast fibroblasts were directly determined from needle biopsy samples. Recently this experimental break-through is published in the renowned *Journal of Proteome Research*.

The potential contribution of stroma cells to [tumour growth](#) has been widely recognised. It is not easy to understand whether a diseased stroma state supports tumour initiation or, alternatively, tumour- stroma cells are responsible for the formation of such diseased stroma. "We successfully identified relevant players as such and analysed these molecules out of human tissue samples for the very first time", says Christopher Gerner, head of the Department of Analytical Chemistry of the University of Vienna. Together with Georg Pfeiler from the Department of Obstetrics and Gynecology of the Medical University of Vienna and an interdisciplinary research team, he has developed the new analysis methodology.

Experimental determination of undesirable tumour promotion by stroma cells

Tissue is made of various cell types, which fulfil different biological tasks. Main components of breast tissue are epithelial cells and fibroblasts. In case of breast cancer, the epithelial cell may transform while the fibroblasts, remaining genetically unaltered, may change their activation state. The typical activity of cancer associated fibroblasts (CAFs) is similar to [wound healing](#) activities. The secreted growth- and survival factors, biologically active at extremely low concentrations, are not only supporting wound healing, but may as well be exploited in case of cancer for further promotion of the disease. The significance of such cell activities has been fully acknowledged only during the last few

years, the current study also presents a relevant in vitro model for more detailed investigations.

Innovative assay based on mass spectrometric analyses of needle biopsies

It was a real analytical challenge to identify the most relevant molecular players out of tissue homogenates which consist of a complex mixture of different kinds of cells together with countless blood constituents. By the use of modern [mass spectrometry](#) several thousand distinct proteins were identified in a first step. Referring to the in vitro model systems mentioned above, it was finally possible to investigate the functional cell state of fibroblasts out of tissue homogenates. This successfully proved that in case of cancer, the fibroblasts display a strong wound healing activity and thus directly promote tumour growth. "This was only possible due to the modern instrumentation I got together with the chair in Bioanalysis", remarks Christopher Gerner referring to the top instruments in the Mass Spectrometry Center of the University of Vienna.

Novel approaches for breast cancer therapy

The results of the current study may have several consequences. Based on [needle biopsies](#), it is now possible to assess functional states of stroma cells. "It is therefore feasible for us to determine to which extent such activities are present and relevant in individual patient samples. This is a first step which may allow us to plan pharmacological interference. However, these are future hopes when referring to clinical practice", says Georg Pfeiler of the Medical University of Vienna. "For that aim we are currently developing an assay using blood serum only", adds Christopher Gerner. Furthermore, it is now possible to use the in vitro model system to test drug candidates interfering with these undesirable

cell activities in a targeted fashion. Clinical application of such an additional therapeutic strategy could substantially improve current therapies with respect to life quality parameters and prognosis.

Currently a team consisting of several PhD-students are working on the realisation of these research projects. Indeed this may typically represent a cross-over project involving experts from bioanalytics, medicine and pharmacology.

More information: *Journal of Proteome Research* (Special Issue: Proteomics of Human Diseases: Pathogenesis, Diagnosis, Prognosis, and Treatment): Proteome Profiling of Breast Cancer Biopsies Reveals a Wound Healing Signature of Cancer-Associated Fibroblasts. Michael Groessl, Astrid Slany, Andrea Bileck, Kerstin Gloessmann, Dominique Kreutz, Walter Jaeger, Georg Pfeiler, Christopher Gerner. September 2014. [DOI: 10.1021/pr500727h](https://doi.org/10.1021/pr500727h)

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