HelmholtzZentrum münchen
Deutsches Forschungszentrum für Gesundheit und Umwelt

Presseinformation

Mini-Breast grown in petri-dishes – a new tool for cancer research

+++ *Embargo: 12th of June 2015, 12:00 noon EST* +++

Neuherberg, 10th of June 2015. **About 70.000 Women are diagnosed with breast cancer every year in Germany alone. Despite significant progress in the treatment of common types of breast cancer, some aggressive subtypes of the disease are poorly understood and remain incurable. A new experimental model opens new avenues for mammary gland biology and basic breast cancer research. Together with their colleagues at the LMU Munich, researchers at the Helmholtz Center in Munich are now able to create three-dimensional organoid-structures that recapitulate normal breast development and function from single patient-derived cells.**

The research group, led by Dr. Christina Scheel, developed an assay whereby cultured human breast epithelial cells rebuild the three-dimensional tissue architecture of the mammary gland. For this purpose, a transparent gel is used in which cells divide and spread, similar to the developing mammary gland during puberty. Specifically, cells divide and generate hollow ducts that form a network of branches and terminate in grape-like structures. Throughout the reproductive lifespan of a woman, the mammary gland is constantly remodeled and renewed in order to guarantee milk production even after multiple pregnancies. Although their exact identity remains elusive, this high cellular turnover requires the presence of cells with regenerative capacity, i.e. stem cells. Breast cancer cells can adopt properties of stem cells to acquire aggressive traits. To determine how aggressive traits arise in breast cancer cells, it is therefore crucial to first elucidate the functioning of normal breast stem cells. For this purpose, the Scheel group provides a new powerful experimental tool.

„A technological break-through"

Using their newly developed organoid assay, the researchers observed that the behaviour of cells with regenerative capacity is determined by the physical properties of their environment. Jelena Linnemann, first author of the study, explains: „We were able to demonstrate that increasing rigidity of the gel led to increased spreading of the cells, or, said differently, invasive growth. Similar behaviour was already observed in breast cancer cells. Our results suggest that invasive growth in response to physical rigidity represents a normal process during mammary gland development that is exploited during tumor progression." Co-author Lisa Meixner adds that „with our assay, we can elucidate how such processes are controlled at the molecular level, which provides the basis for developing therapeutic strategies to inhibit them in breast cancer."

Another reason the mini-mammary glands represent a particularly valuable tool is, because the cells that build these structure are directly isolated from patient tissue. In this case, healthy tissue from women undergoing aesthetic breast reduction is used. Co-author Haruko Miura explains: "After the operation, this tissue is normally discarded. For us, it is an experimental treasure chest that enables us to tease out individual difference in the behavior of stem and other cells in the human mammary gland."

Experimental models that are based on patient-derived tissue constitute a corner stone of basic and applied research. "This technological break-through provides the basis for

many research projects, both those aimed to understand how breast cancer cells acquire aggressive traits, as well as to elucidate how adult stem cells function in normal regeneration", says Christina Scheel, head of the study.

More Information

Background

In Germany, one in eight women is going to be diagnosed with breast cancer throughout her lifetime. In the past 30 years, the rate of newly diagnosed breast cancer cases has doubled. The reasons for this increase are unclear. Despite this greatly increased rate, mortality is declining steadily due to improved early detection and therapeutic options. Nonetheless, some aggressive subtypes of breast cancer remain poorly understood and incurable. The aggressive behaviour of these breast cancer cells most likely originates in how the mammary gland develops and functions. The mammary gland itself consists of a structure similar in form to a bunch of grapes: a number of branching hollow ducts terminate in tiny, milk-producing pouches on one end, and the nipple on the other. This network of ducts in embedded in fatty and connective tissue which lends the breast is overall form. The mammary gland is the name-giving characteristic of mammals and provides a massive evolutionary advantage for raising offspring. From a developmental point-of-view it is therefore essential that the highly energy-intensive process of milk production kicks in after each pregnancy. It is thought that for this purpose, the mammary gland harbours stem cells that are able to regenerate the entire mammary gland. However, how exactly such stem cells contribute to the main developmental phase of the mammary gland during puberty is not entirely clear. Without doubt, aggressive breast cancer cells activate developmental processes in an uncontrolled manner, which impacts many aspects of tumor progression. In that sense, a tumor is like an uncontrolled, regenerating organ. Importantly, elucidating how these regenerative processes are normally controlled provide the basis for the development of new targeting strategies.

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The **Helmholtz Zentrum München**, the German Research Center for Environmental Health, pursues the goal of developing personalized medical approaches for the prevention and therapy of major common diseases such as diabetes and lung diseases. To achieve this, it investigates the interaction of genetics, environmental factors and lifestyle. The Helmholtz Zentrum München is headquartered in Neuherberg in the north of Munich and has about 2,300 staff members. It is a member of the Helmholtz Association, a community of 18 scientific-technical and medical-biological research centers with a total of about 37,000 staff members.

The **Institute of Stem Cell Research (ISF)** investigates the basic molecular and cellular mechanisms of stem cell maintenance and differentiation. From that, the ISF then develops approaches in order to replace defect cell types, either by activating resting stem cells or by re-programming other existing cell types to repair themselves. The aim of these approaches is to stimulate the regrowth of damaged, pathologically changed or destroyed tissue.

The research objective of the **Institute of Experimental Genetics** (IEG) is to elucidate the causes and pathogenesis of human diseases. Due to its prominent role in interdisciplinary and international consortia, the IEG is a global leader in the systemic study of mouse models for human diseases and the elucidation of involved genes. The main focus is on metabolic diseases such as diabetes. The IEG is part of the Helmholtz Diabetes Center (HDC).

As one of Europe's leading research universities, **LMU Munich** is committed to the highest international standards of excellence in research and teaching. Building on its 500-year-tradition of scholarship, LMU covers a broad spectrum of disciplines, ranging from the humanities and cultural studies through law, economics and social studies to medicine and the sciences. 15 percent of LMU's 50,000 students come from abroad, originating from 130 countries worldwide. The know-how and creativity of LMU's academics form the foundation of the University's outstanding research record. This is also reflected in LMU's designation of as a "university of excellence" in the context of the Excellence Initiative, a nationwide competition to promote top-level university research.

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Image Credit: Haruko Miura. Detail of breast epithelial cells in culture undergoing ductal elongation and side-branching.