

Shell-less chicken eggs for multiple myeloma research

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Myelom

Innsbruck scientists grow miniature tumours on eggshell membranes. The EU project OPTATIO succeeded in developing an urgently needed drug screening system for bone marrow cancer.

Multiple myeloma is an incurable cancer of the <u>bone marrow</u>. To date, no screening systems have been available to examine the effects of new



drugs in a 3D environment. Researchers on the EU project OPTATIO might now fill this gap. They succeeded in growing miniature human myelomas in shell-less chicken eggs in order to screen new marine compounds for anti-myeloma activity. Recently, several of the drug candidates showed promising results. Now Dr. Gerold Untergasser of Innsbruck Medical University together with colleagues and international cooperation partners reveals to a broader public how their assay works. A video publication was released this week in the current issue of the *Journal of Visualized Experiments*.

Multiple myeloma is a malignant disease that affects a certain kind of immune <u>cells</u>, the plasma cells in the bone marrow. They proliferate extensively, thereby damaging bones, blood formation and the immune system in general. Treating the mostly elderly patients is complicated by the profound heterogeneity of this type of cancer. Its progression varies greatly from patient to patient and the tumour cells quickly become therapy-resistant. A broad range of drugs with different targets and modes of actions would help improve patient outcome. Since 2012 the European research consortium OPTATIO (OPtimizing TArgets and Therapeutics In high-risk and refractOry Multiple Myeloma) has taken on this serious problem.

Dr. Untergasser and his colleagues at the Department of Hematology and Oncology (lead by Prof. Günther Gastl) of Innsbruck Medical University transfect human myeloma cells with the shiny green jellyfish protein GFP. The marked cells are easy to recognize and observe through a fluorescence microscope. The researchers cultivate the <u>tumour cells</u> together with human mensenchymal cells from the bone marrow and collagen in the shape of three-dimensional cell spheres, thereby simulating the natural microenvironment of the tumour in the bone marrow that plays a crucial role in <u>multiple myeloma</u>. After removing the egg shells, the researchers transfer their little cell spheres to the outer membrane. The so-called choriallantoid membrane provides a perfect



base for growing miniature human tumours in a petri dish.

This assay allows researchers to add putative antimyeloma drugs and observe whether they are able to specifically kill myeloma cells. This is not an easy task because the surrounding mensenchymal cells protect the tumor in the test system just as they do in patients. Cancer drugs have to overcome this protective shield. Additionally, the researchers examine whether the test substances are able to prevent the tumour from attracting new blood vessels. Finally, the scientists also learn about the drug's toxicity for the entire organism.

Gerold Untergasser: "The chicken egg is much easier to handle and cheaper than mice and it reduces the number of animal experiments. In our new video publication we give detailed information on how our system works. We provide an easy-to-repeat protocol for broad use within the research community. Our vision for the future is that a separate test is performed for each patient to determine which drug is best suitable."

Dr. Wolfgang Willenbacher, scientific coordinator of OPTATIO, states: "The interdisciplinary character of the consortium, which is composed of clinics, companies and academia, has proven very fruitful. Development of the CAM assay for <u>drug screening</u> is a perfect example: The researchers in Prof. Domenico Ribatti's group at the University of Bari contributed their expertise on blood vessel formation, our clinical partners supported us with patient samples, the Spanish pharmaceutical company PharmaMar provided test substances from marine organisms and the researchers at Innsbruck Medical University developed the new screening system together with Oncoctyrol – Center for Personalized Cancer Medicine and the Tyrolean Cancer Research Institute."

Dr. Willenbacher looking back on the three-year project: "OPTATIO's goal was to better understand the microenvironment of multiple



myeloma and to find out how we can make therapeutical use of this knowledge. The European cooperation enabled us to lay valuable foundations for future research, especially in setting up registries and developing new drug screening systems."

More information: "Marine compounds inhibit growth of multiple myeloma in vitro and in vivo" *Oncotarget*, 6(10), 8200-8209. Retrieved from <u>www.impactjournals.com/oncotar ... article&op=view&path</u> %5B%5D=3362

"Establishment of a Human Multiple Myeloma Xenograft Model in the Chicken to Study Tumor Growth, Invasion and Angiogenesis", *Journal of Visualized Experiments*, Issue 99, 2015 DOI: 10.3791/52665 (2015).

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