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ReImaging Breasts

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IMAGING HUMAN BREAST TUMOURS IN DIFFERENT SPECIES: HOW HUMAN ARE THEY?

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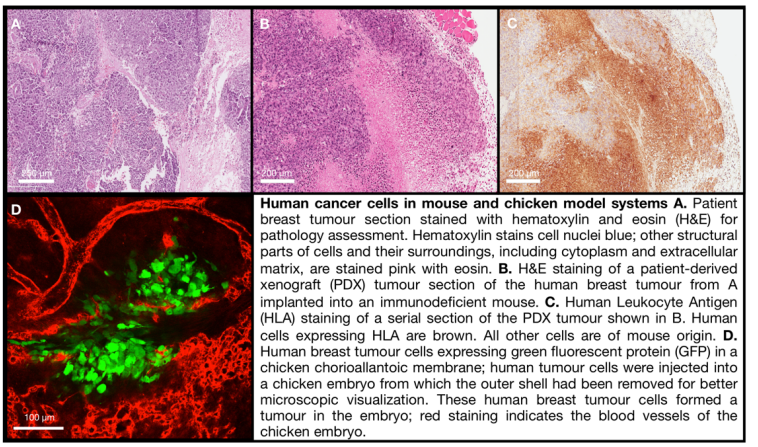
***Abstract**: In a gedankenexperiment, we pose the philosophical question as to whether human breast cancer cells or tissues can still be considered human after transplantation into another species. Alongside medical research images illustrating xenotransplantation, we provide descriptions of how tissues were prepared for imaging. In addition, we discuss how such models enable further understanding of cancer and provide invaluable tools for testing new therapies.*

***Resume** : Dans un gedankenexperminent nous posons la question philosophique de savoir si les tissus et cellules de cancer du sein humain peuvent toujours être considérés comme humains après qu'ils ont été transplantés dans une autre espèce. En plus de photographies de recherche médicale illustrant la xénotransplantation, nous offrons des descriptions expliquant comment des tissus ont été préparés pour la visualisation. Nous débattons en outre de la manière dont de tels modèles permettent une meilleure compréhension du cancer et offrent des outils inestimables pour tester de nouvelles thérapeutiques.*

Cancer researchers use model systems in order to understand mechanisms of cancer initiation and progression, and also to test new treatments. This is done before such treatments are tested in people, and is governed by the Helsinki Declaration (World Medical Association) as well as national animal care committee guidelines (such as those of the CCAC in Canada, OLAW in the USA,

and GV-Solas in Germany), which ensure ethical practices are employed in the use of both human tissues and animals in research.

Xenograft (xenos, Greek = foreign) models involve transplanting human cells or tissue into mice that have little to no immune systems (which would reject the transplants). For diagnostic purposes, pieces of breast tumours removed during surgeries are preserved and sent to histology labs for processing. Tumours are embedded in paraffin and sliced very thinly, after which these "sections" are stained with hematoxylin and eosin (H&E) dyes. These allow pathologists to see the sizes and shapes of cells under the microscope, to distinguish cell nuclei from other structures within the cell and also to identify structures outside of cells, termed extracellular matrix. An example of an H&E stained section of a human tumour is shown in panel A. The corresponding H&E section from the model system derived from this very tumour—the patient derived xenograft (PDX, Charles River)—is depicted in panel B. The similarities are striking, and therein lies the power of the PDX. The human tumour piece has been implanted into a mouse, allowed to grow in size, and then pieces thereof are further implanted into more mice. Throughout this process, these tumour pieces retain most characteristics of the original malignancy; this enables creation of a tissue bank that can be used for testing promising anti-cancer drugs and immunotherapies.



Human cancer cells in mouse and chicken model systems A. Patient breast tumour section stained with hematoxylin and eosin (H&E) for pathology assessment. Hematoxylin stains cell nuclei blue; other structural parts of cells and their surroundings, including cytoplasm and extracellular matrix, are stained pink with eosin. **B.** H&E staining of a patient-derived xenograft (PDX) tumour section of the human breast tumour from A implanted into an immunodeficient mouse. **C.** Human Leukocyte Antigen (HLA) staining of a serial section of the PDX tumour shown in B. Human cells expressing HLA are brown. All other cells are of mouse origin. **D.** Human breast tumour cells expressing green fluorescent protein (GFP) in a chicken chorioallantoic membrane; human tumour cells were injected into a chicken embryo from which the outer shell had been removed for better microscopic visualization. These human breast tumour cells formed a tumour in the embryo; red staining indicates the blood vessels of the chicken embryo.

The question arises, however, as to whether human breast cancer cells or breast tumour tissues can still be considered human after they have been transplanted into another species, such as a mouse or chicken embryo. To survive in another species, a human tumour must connect with the blood system of that species, which allows various support cells to enter the tumour and help it thrive. So how human is the tumour at this point?

One defining feature of human cells is their expression of specific proteins called human leukocyte antigens (HLA) on their surface (World Health Organization, Park and Terasaki). Using a technique called immunohistochemistry, we can detect the presence or absence of HLA on cells in tumour sections. HLA expression on the tumour in panel B is shown in panel C: brown staining indicates the presence of human HLA and the lack of stain indicates mouse cells. Thus, the breast tumour, that looks so similar to its all-human counterpart in A, has now become a hybrid of human and mouse.

Another type of xenograft model used in breast cancer research is the chicken chorioallantoic membrane (CAM) model (Nowak-Sliwinka et al.). Egg shells are removed from chicken embryos so that we can visualize them easily using a microscope. Human cancer cell lines are often engineered in the lab to produce a fluorescent protein, so that they can be easily distinguished from the host (mouse or chicken, in this case) and monitored using different types of imaging techniques. These are then injected into the CAM and are used to learn about many aspects of cancer progression. Panel D shows human breast cancer cells that express green fluorescent protein (GFP) that have formed a tumour in a CAM; here, the circulation system of the chicken embryo has been dyed red (rhodamine bound to lectin on the cell surface). Again, the chicken cells and system support human tumour growth, allowing us to study aspects of breast cancer and how metastasis occurs (Leong et al.).

How human are these breast tumours? It is a question worth considering. For now, we can at least say that they are human enough for us to learn more about human breast cancer, and test new treatments that will hopefully lead to better outcomes for breast cancer patients.

WORKS CITED

Charles River. "When and Where to Add PDX Models: IO and Non-IO." Webinar: https://www.criver.com/resources/webinar-pi-ds-when-and-where-add-pdx-models-io-and-non-io

Leong, H.S. et al. "Assessing cancer cell migration and metastatic growth in vivo in the chick embryo using fluorescence intravital imaging." *Methods in Molecular Biology*, vol. 872, 2012, pp. 1-14, doi: 10.1007/978-1-61779-797-2_1.

Nowak-Sliwinska, P. et al. "The chicken chorioallantoic membrane model in biology, medicine and bioengineering." *Angiogenesis*, vol. 17, no. 4, 2014, pp. 779-804, doi: 10.1007/s10456-014-9440-7.

Park, I. and P. Terasaki. "Origins of the first HLA specificities." *Hum Immunology*, vol. 61, no. 3, 2000, pp. 185-89, doi: 10.1016/s0198-8859(99)00154-8.

World Health Organization. "Nomenclature for factors of the HL-a system." *Bulletin of the World Health Organization,* vol. 39, no. 3, 1969, pp. 483-86.

World Medical Association. "World Medical Association Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects." *JAMA*, vol. 310, no. 20, 2013, 2191-94, doi: 10.1001/jama.2013.281053.