

The advantages of the patient-derived orthotopic xenograft (PDOX) mouse models of cancer

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A great breakthrough in cancer research was made when Rygaard and Povlsen subcutaneously implanted the first human patient tumor in nude mice in 1969 and passaged it in nude mice 77 times. For the first time, human tumors could be consistently grown in a mouse model. To this day, researchers are doing similar subcutaneous implantation of tumors in immunodeficient mice. However, subcutaneously-implanted tumors almost never metastasize. Thirteen years later in 1982, Sordat made the first orthotopic nude-mouse model of cancer using colon cancer cells. Sordat observed cancer cell invasion, not observed with subcutaneous implantation. In 1991, our laboratory published the first patient-derived orthotopic xenograft (PDOX) model using surgical orthotopic implantation (SOI) in nude mice which enabled for the first time a patient tumor mouse model to mimic the patient. PDOX models have been established with all major cancer types enabling the discovery and evaluation of novel therapeutics, including anti-metastatic and anti-stromal agents, as well as individualized therapy of cancer patients.

Major publications

1. Fu, X., Besterman, J.M., Monosov, A., and Hoffman, R.M. Models of human metastatic colon cancer in nude mice orthotopically constructed by using histologically intact patient specimens. *Proc. Natl. Acad. Sci. USA* 88, 9345-9349, 1991.
2. Fu, X., Guadagni, F., and Hoffman, R.M. A metastatic nude-mouse model of human pancreatic cancer constructed orthotopically from histologically intact patient specimens. *Proc. Natl. Acad. Sci. USA* 89, 5645-5649, 1992.
3. Yang, M., Baranov, E., Jiang, P., Sun, F-X., Li, X-M., Li, L., Hasegawa, S., Bouvet, M., Al-Tuwaijri, M., Chishima, T., Shimada, H., Moossa, A.R., Penman, S., Hoffman, R.M. Whole-body optical imaging of green fluorescent protein-expressing tumors and metastases. *Proc. Natl. Acad. Sci. USA* 97, 1206-1211, 2000.
4. Hoffman, R.M. The multiple uses of fluorescent proteins to visualize cancer in vivo. *Nature Reviews Cancer* 5, 796-806, 2005.
5. Hoffman, R.M. Patient-derived orthotopic xenografts: better mimic of metastasis than subcutaneous xenografts. *Nature Reviews Cancer* 15, 451-452, 2015.
6. Hoffman, R.M., ed. Patient-Derived Mouse Models of Cancer. *Molecular and Translational Medicine*. Coleman, W.B., Tsongalis, G.J., Series eds. Springer Intl. Publishing AG, 2017. ISSN:2197-7852.
7. Hoffman, R.M. Orthotopic metastatic mouse models for anticancer drug discovery and evaluation: a bridge to the clinic. *Investigational New Drugs* 17, 343-359, 1999.



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1965 State University of New York (Buffalo, New York), B.A. (Biology)
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PREVIOUS ACADEMIC POSITIONS:

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