

# The unique benefits of patient-derived orthotopic xenograft (PDOX) mouse models of cancer

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Rygaard in 1969 was able to establish a patient colon cancer obtained at surgery subcutaneously in nude mice and passaged it over 70 times. Rygaard's technique of subcutaneously implanting patient tumors in nude mice spread all over the world to numerous laboratories. However such models with tumors growing subcutaneously rarely metastasized even if the tumor was highly metastatic in the patient. The subcutaneous micro-environment is not permissive for metastasis of organ tumors. Sordat in 1982 developed an orthotopic model by implanting human colon cancer cells to the colon of nude mice and observed cancer-cell invasion. We developed the technique of surgical orthotopic implantation (SOI) which allowed patient-like metastasis and drug response of patient tumors in nude mice. We termed this model the patient-derived orthotopic xenograft (PDOX). We have also observed orders of magnitude differences in gene expression between the same tumor implanted orthotopically or subcutaneously. We have also demonstrated efficacy of transformational therapy in PDOX models with tumor-targeting bacteria and methioninase. Recently we have demonstrated a very high establishment rate of patient tumors in nude mice with a new technique which should allow the establishment of a PDOX model for most patients with cancer, a revolution for individualized precision therapy.

## 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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### EDUCATION:

1965 State University of New York (Buffalo, New York), B.A. (Biology)  
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### POSTDOCTORAL TRAINING:

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1978 Weizmann Institute of Science Rehovot, Israel

### PREVIOUS ACADEMIC POSITIONS:

1975-1979 Instructor of Pediatrics, Harvard Medical School Massachusetts General Hospital  
1979-1983 Assistant Professor, Department of Pediatrics University of California, San Diego School of Medicine  
1983-1990 Associate Professor, Department of Pediatrics University of California, San Diego School of Medicine  
1990-1995 Professor, Department of Pediatrics University of California, San Diego School of Medicine

### PRESENT POSITIONS:

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