INOVOTION Tests for drug discovery : Early Identification of Low Value Leads

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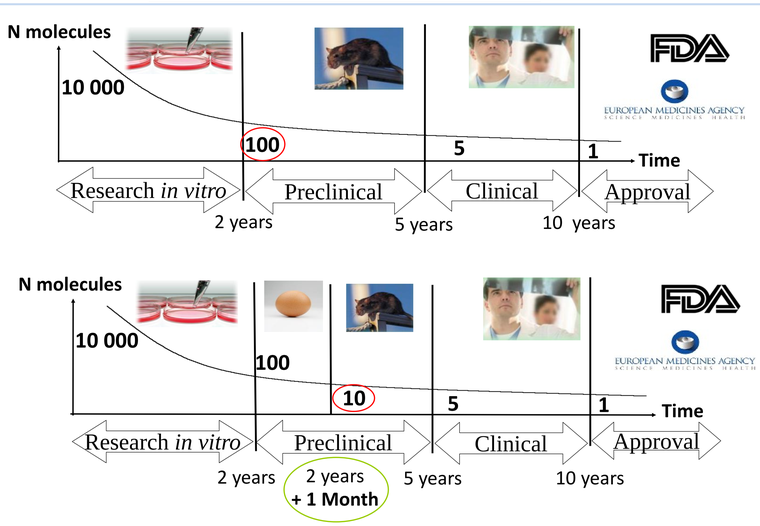
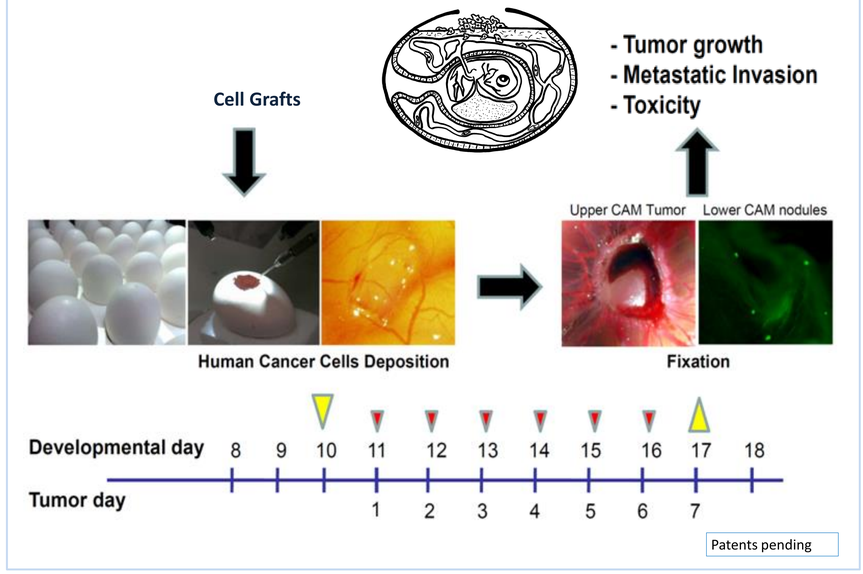
Abstract

Since its introduction, the chick embryo model involving the technique of chorioallantoic grafting has proved extremely valuable for the in vivo studies of tumor development, angiogenesis and malignant cell dissemination. The ability of the chick embryo's chorioallantoic membrane (CAM) to efficiently support the growth of inoculated xenogenic tumor cells greatly facilitates the analysis of human tumor cell metastasis. We have developed highly sensitive and reproducible assays for monitoring the growth and the metastatic dissemination of human tumor cells in the chick embryo. These tests are validated for 12 human tumors cell lines including various carcinomas, gliomas and melanomas as well as reference drugs currently marketed. Using these assays we can investigate the efficacy and the toxicity of new drug lead candidates in oncology. These assays can also be used to study genetically modified cell lines. The data obtained with this model are much faster, more reliable, less expensive and need only minute amounts of drug (>1,000 times less) compared to the mouse model. Our tests are applicable to any preclinical anti-cancer drug discovery program. Moreover, they could be used for the early evaluation of the toxicity of any new drug candidates, i.e. not just in oncology. Altogether, our tests make the chick embryo CAM system an attractive model to reduce animal experimentation for drug discovery.

Early Identification of Low Value Leads



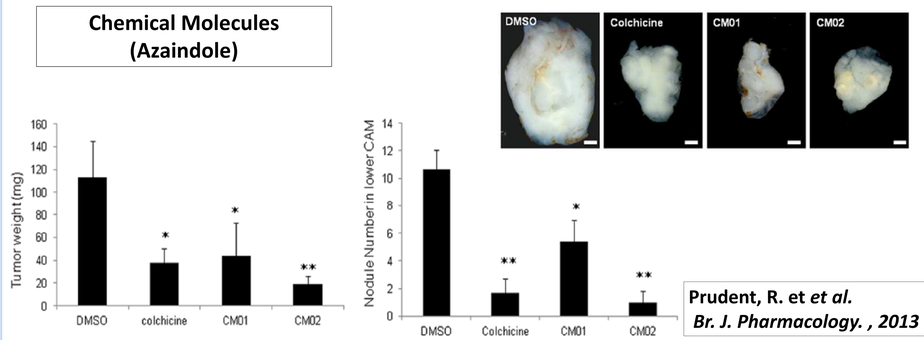


Patents pending

Human Cancer Cell Lines

Breast adenocarcinoma	MDA 231	Paclitaxel
Lung carcinoma	A549	Vinorelbine
Lung carcinoma	H1299	Paclitaxel - Vinorelbin
Cervix adenocarcinoma	Hela	Paclitaxel
Hepatocellular carcinoma	Hep3B	Paclitaxel
Hepatocellular carcinoma	HepG2	Paclitaxel
Colon adenocarcinoma	HT29	Irinotecan
prostatic adenocarcinoma	PC3	Vinorelbine
Glioma	U87	Temozolomide
Glioma	GL261	Temozolomide
Melanoma	B16F10	Paclitaxel - Cyclophosphamide
Rhabdomyosarcoma	RH30	Tamoxifen

Chemical Molecules (Azaindole)



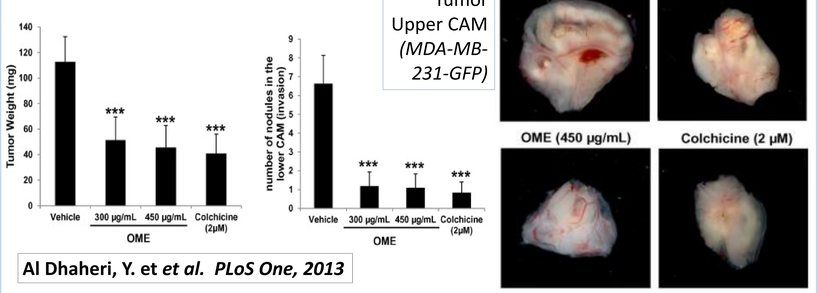
Prudent, R. et *et al.* *Br. J. Pharmacology. , 2013*

Multiple Benefits

Sensitivity - Reliability - Speed - Cost saving

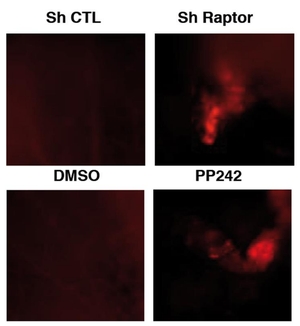
	In Ovo	Mouse
Amount of drug	1 unit	1,000 units
Time to result	20 days	2-3 months
Cost	1	5-10
Analysis	*In vivo*	*In vivo*
N data points/test	30-150	6-12
Animal use	*NO*	*YES*

Natural Compounds



Al Dhaheri, Y. et *et al.* *PLoS One, 2013*

Genetically Modified Cell lines



Nodule or Foci Lower CAM *(MCF10A)*

	nb of egg with invaded lower CAM	mean foci nb / egg	s.d.
MCF10A Sh-CTL	0/10	0	0
MCF10A Sh-Raptor	7/10	2.57	0.90
MCF10A DMSO	0/10	0	0
MCF10A PP242	8/10	2.63	1.58

Mikaelian, I. *et al. Cancer Research, 2013*

References:

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