# A preclinical platform for drug evaluation on a RANKL - dependent breast cancer mouse model: *in vivo* monitoring through PET screening

BreastCaRANKL

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## Introduction

Breast cancer is one of the most common cancer types worldwide and there is a strong need to develop new personalized targeted treatments. The receptor activator of NF-κB ligand RANKL/RANK system is essential for the development and activation of osteoclasts as well as the initiation of specific types of breast cancer supporting progesterone-driven proliferation of mammary gland epithelial cells[1].

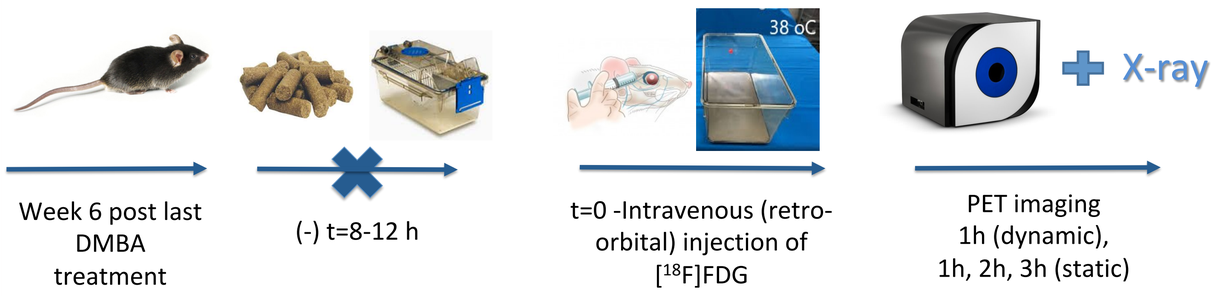
## Objectives

In the frame of this study, mammary carcinogenesis was induced in transgenic mice overexpressing human RANKL (TgRANKL)[2] as well as in wild-type (WT) littermates, using combined treatment, with slow release medroxyprogesterone acetate (MPA) pellets and DNA-damaging agent DMBA[1], in order to establish a preclinical platform for the non-invasive evaluation of human therapeutics targeting the innovative human RANKL-dependent breast cancer.

## Materials and Methods

To establish diagnostic tools for tracking cancer progression, three to six weeks after the last DMBA treatment, palpable tumors, evident in most of the mouse groups (WT, TgRANKL, TgRANKL receiving treatment with anti-RANKL) were analyzed through real-time, dynamic *in vivo* whole-body 2D positron emission tomography (PET) scanning technology (β-eye™, BIOEMTECH) with the clinically approved tracer 2-deoxy-D-[$^{18}$F] fluoroglucose ([$^{18}$F]FDG). The uptake and metabolism of [$^{18}$F]FDG is higher in cancer than in normal cells because of the increased glycolysis and overexpression of glucose membrane transporters (GLUTS)[3]. Therefore, it could serve as a useful tool also for the diagnosis, staging and therapy monitoring of this kind of tumor.

**WT or TgRANKL**




Week 6 post last DMBA treatment

(-) t=8-12 h

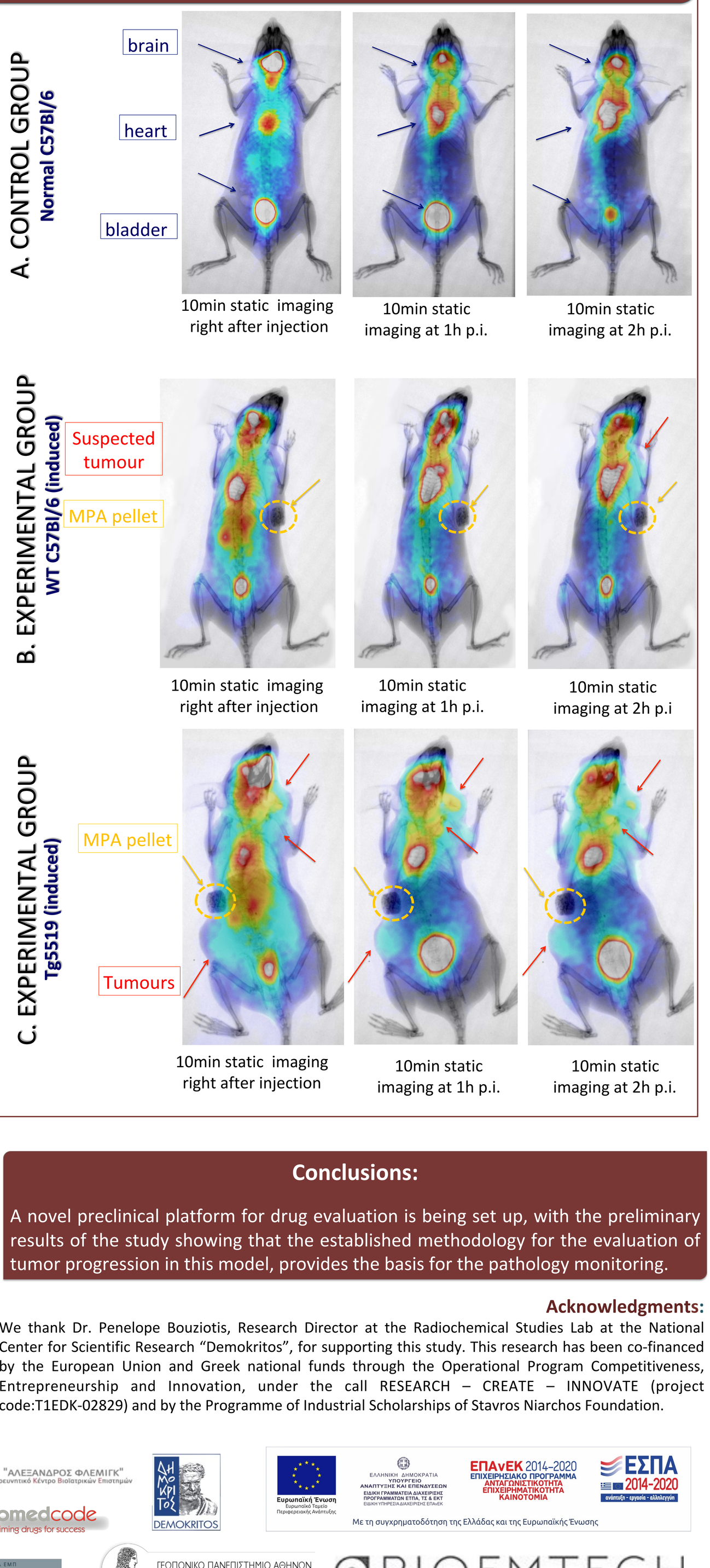
t=0 -Intravenous (retro-orbital) injection of [$^{18}$F]FDG

PET imaging 1h (dynamic), 1h, 2h, 3h (static)

## Results & Discussion

**Real time, dynamic 2D PET and X-ray** imaging results of normal female **C57BL/6** mice (**Control group**) **(A)** and of **WT** (**B) Tg5519** (**C**) female mice (**Experimental group**) on week 6 post last DMBA treatment, at 1h and 2h (static) post-injection, p.i. (~100ul/30uCi, retro-orbital sinus) are presented. Detected tumors are mostly located either on the 1$^{st}$ or 2$^{nd}$ (namely cervical; right) or the 4$^{th}$ (namely inguinal; left) pair of mammary glands (tumour area delineated with a red arrow). Ongoing experiments are elucidating the anti-tumor efficacy via a combined inhibition of human and mouse RANKL.

## Figures




## Conclusions:

A novel preclinical platform for drug evaluation is being set up, with the preliminary results of the study showing that the established methodology for the evaluation of tumor progression in this model, provides the basis for the pathology monitoring.

**Bibliography:**

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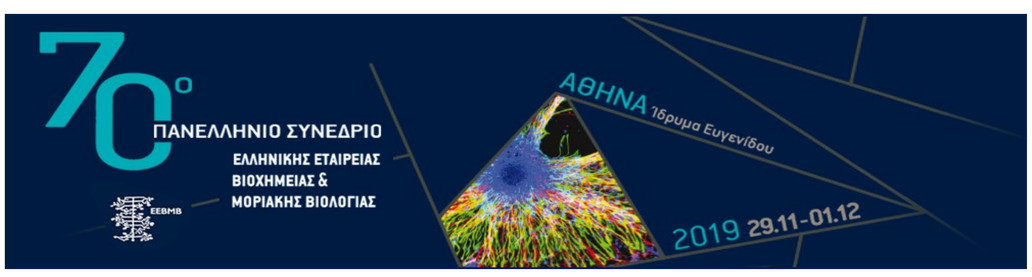
2. Rinotas et al. Journal of Bone and Mineral Research (2014) 29 (5): 1158–1169
3. Penuelas et al. Journal of Oncology (2012) Article ID 710561, 9 pages

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