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TARGETING HER3 IN CANCER THERAPY: PIONEERING APPROACHES THROUGH DNA VACCINATION AND MONOCLONAL ANTIBODY DEVELOPMENT

Laura Luberto, Alessia Muzi , Fabiana Fosca Ferrara , Roberto Arriga , Manuela Cappelletti , Antonella Conforti , Emanuele Marra, Luigi Aurisicchio and Roscilli Giuseppe

Takis Internal Research

CONFERENCE
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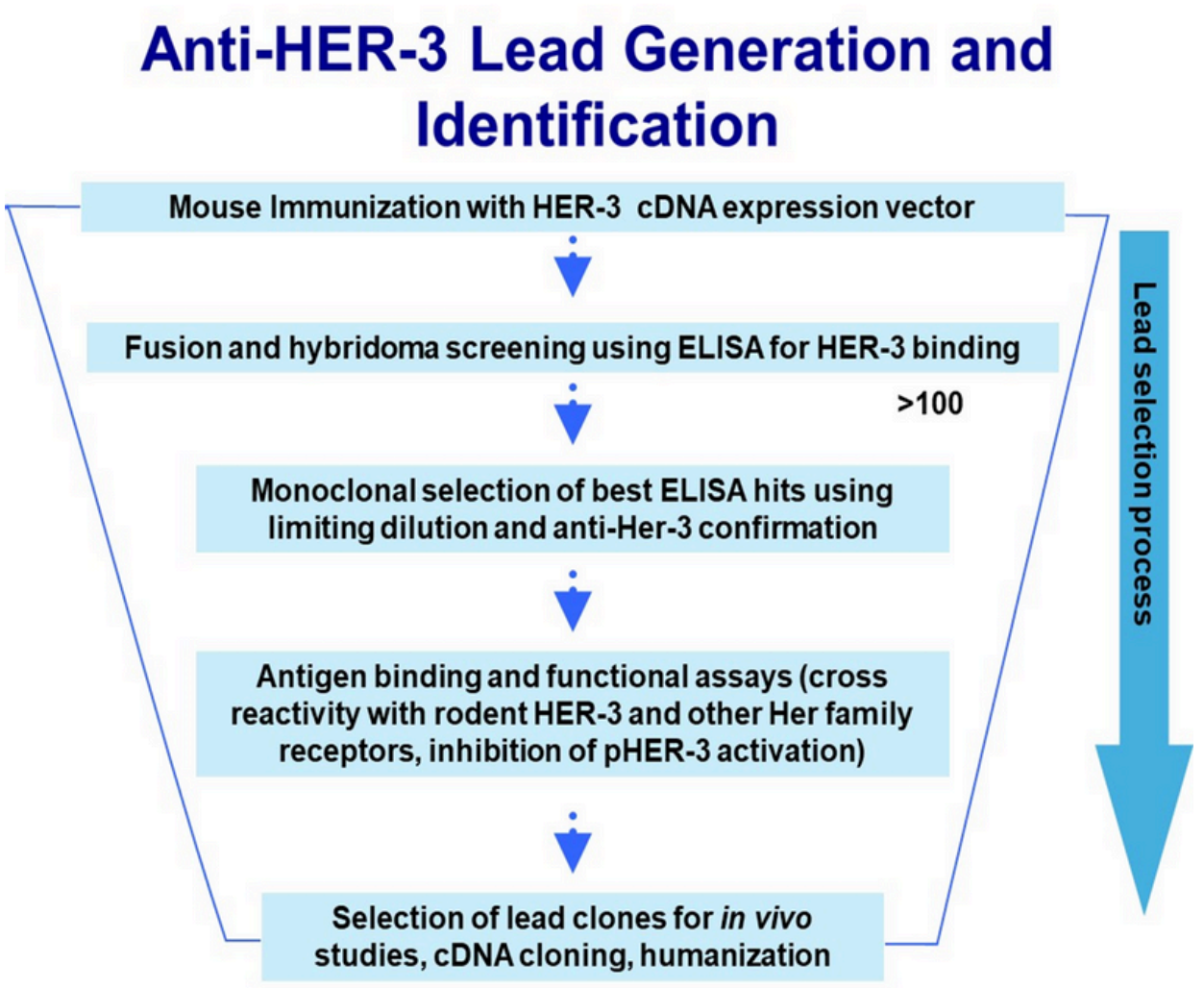
THE PIPELINE

- **Extracellular/transmembrane domains** (HER3_ECD-TM), **delivered via DNA electro-gene-transfer** (DNA-EGT) into BALB/NeuT **mice**.

- Generating of a **series of hybridomas against human ErbB3** through DNA-EGT. **Antibodies selected** for their ability to inhibit the ErbB3-mediated signalling pathway effectively

- **Anti-ErbB3 monoclonal antibodies** demonstrated in vitro growth **modulation of cancer cells** and in vivo **antitumor properties** across various cancer models



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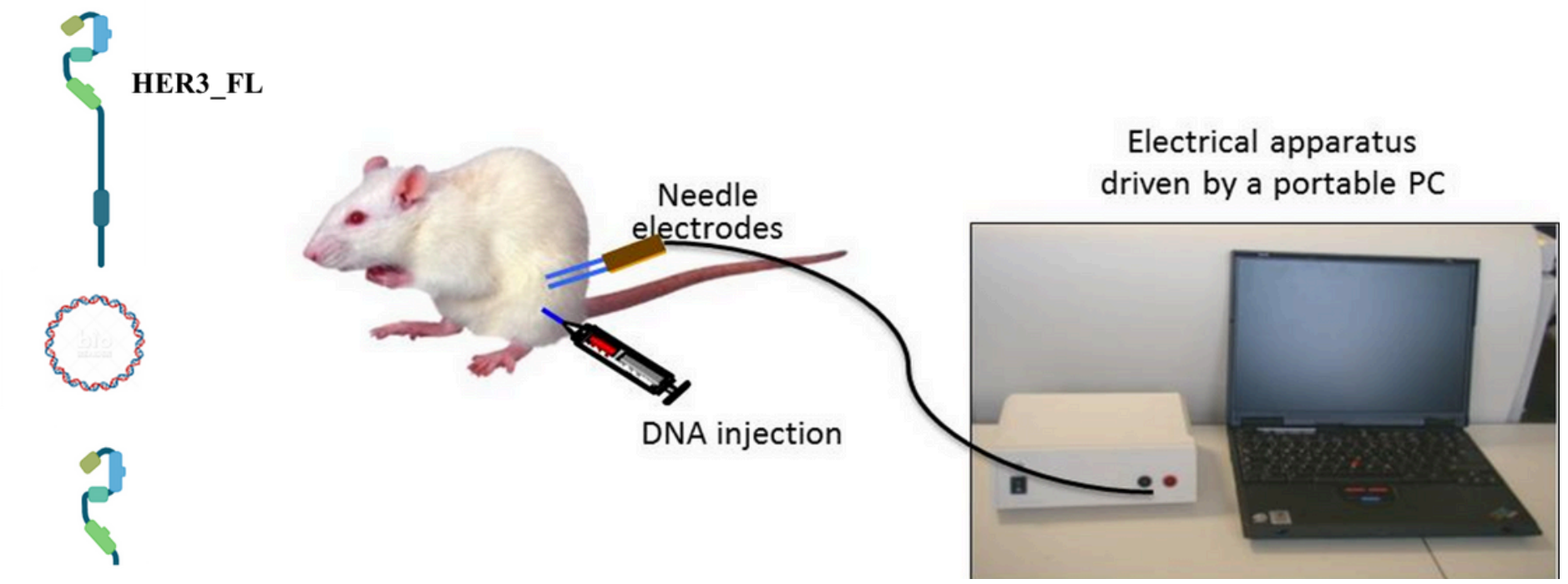
THE AIM

Our research aims to introduce a **dual-pronged approach targeting HER3** through a therapeutic vaccine and a novel **monoclonal antibody strategy**, with potential extensions to vectorized antibody expression and advanced antibody-based therapeutics.



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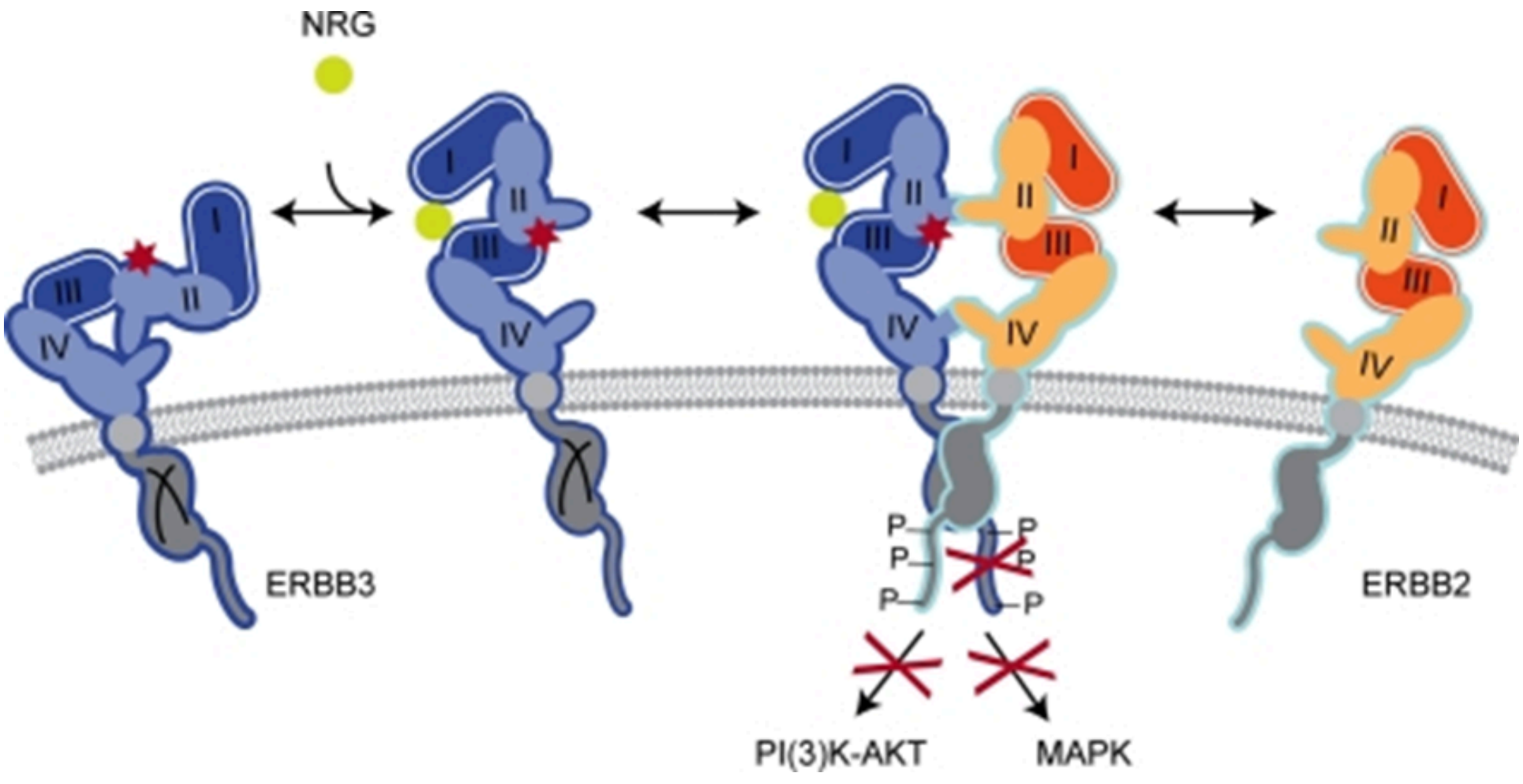
THE ROLE OF THE HER3 RECEPTOR

The **human epidermal growth factor receptor 3** (ErbB3 or HER3), a pivotal member of the ErbB receptor family, is **integral to cellular regulation and oncogenesis**, particularly in mediating drug resistance. The role of the **HER3 receptor** in signal transduction is to **augment the signaling repertoire of active heterodimeric ErbB** receptor complexes by **activating the PI3K/AKT pathway**, which in turn **promotes survival and proliferation**. This positions HER3 as a strategic target for innovative cancer therapies.



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METHODS & RESULTS

We developed a **genetic cancer vaccine employing DNA vectors encoding** either the full length of **HER3** (HER3_FL) or its extracellular/transmembrane domains (HER3_ECD-TM), delivered via DNA electro-gene-transfer (DNA-EGT) into BALB/NeuT mice. This method is designed to **induce a specific immune response against tumor cells**, establishing long-term immunologic memory to prevent cancer relapse.

Concurrently, we **explored a monoclonal antibody strategy**, generating a series of hybridomas against human ErbB3 through DNA-EGT. These **antibodies were selected for their ability to inhibit the ErbB3**-mediated signalling pathway effectively

Our **results** show that **DNA-EGT vaccination elicited a robust immune response against HER3**, significantly preventing cancer onset in prophylactic settings and **slowing tumor progression** in therapeutic models. Moreover, the **anti-ErbB3 monoclonal antibodies demonstrated** in vitro growth modulation of cancer cells and **in vivo antitumor properties** across various cancer models.

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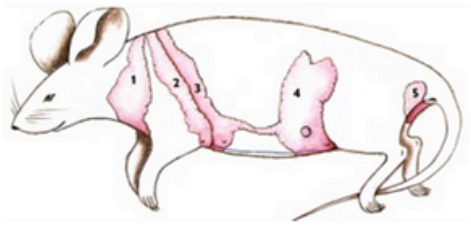
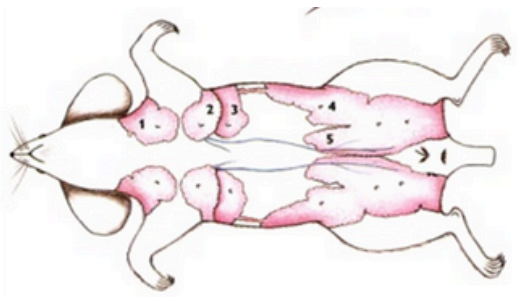
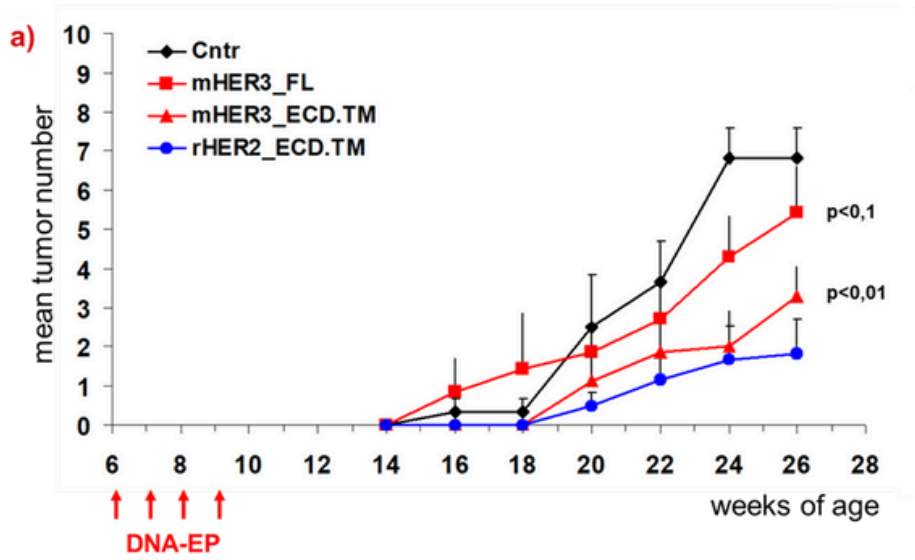
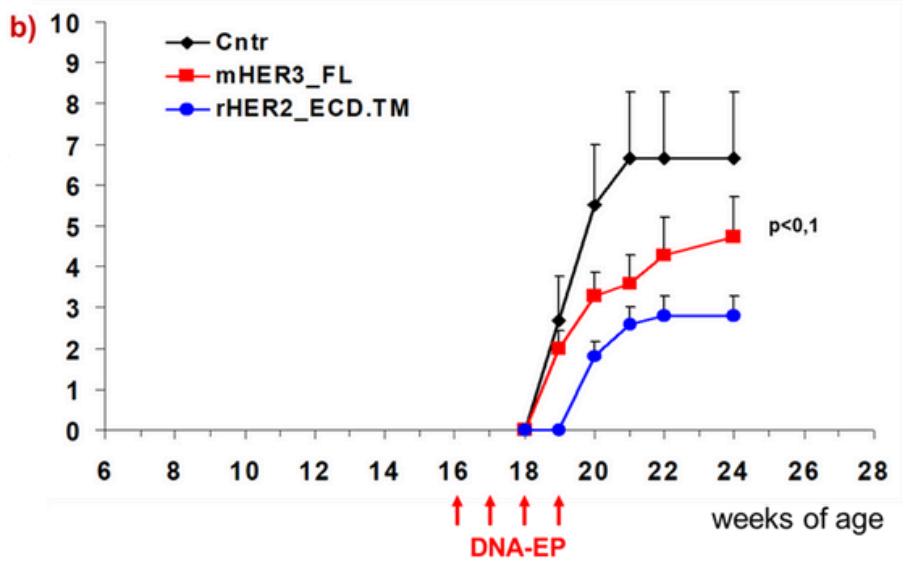
RESULTS









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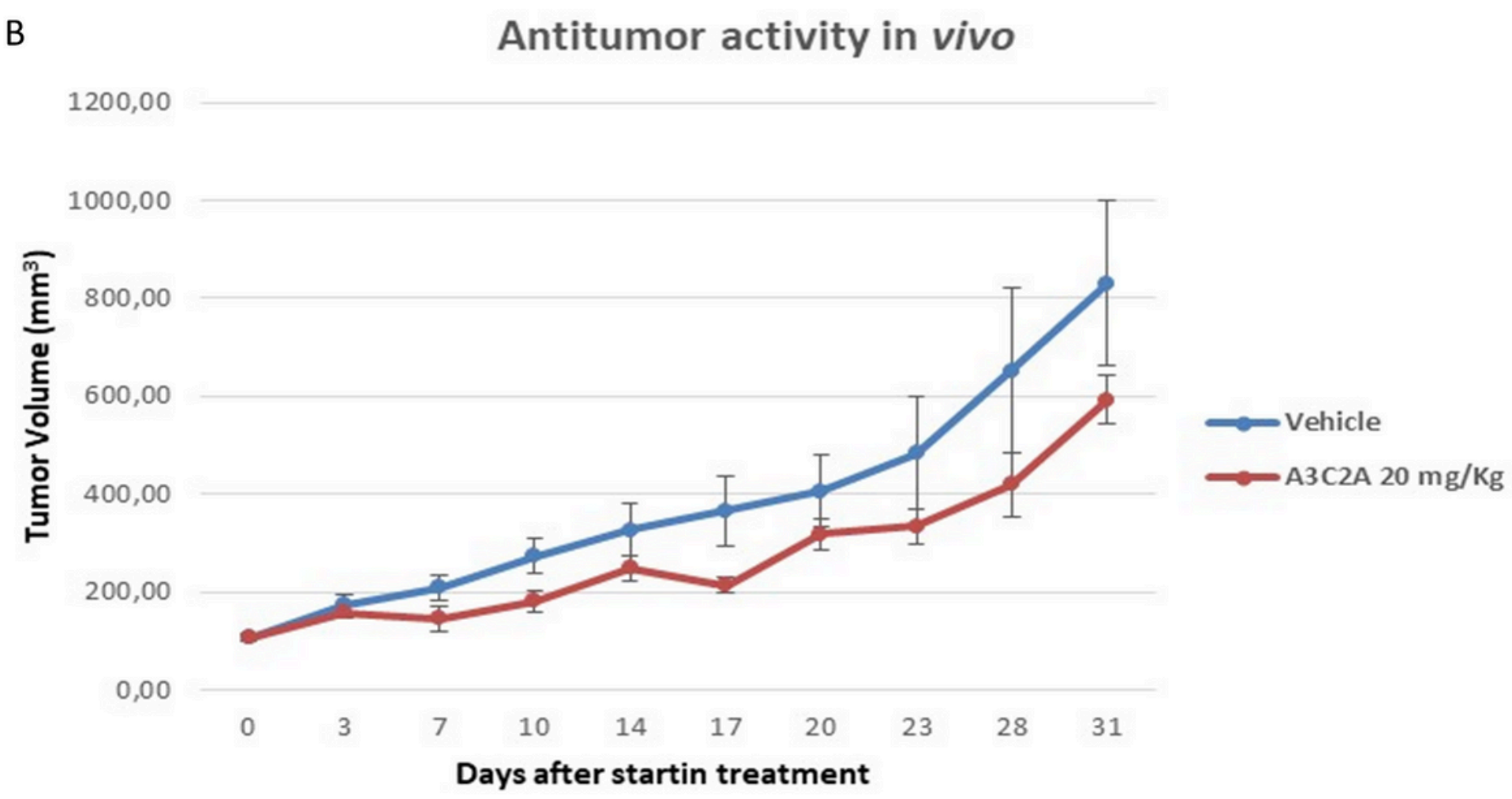

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OUTLOOKS

- **Prophylactic**: mice were treated with 4 sequential DNA-EP before the 10th week of age; **mHER3_ECD.TM vaccine** was able to **prevent significantly cancer occurrence**;

- **Therapeutic**: mice were immunized at 16° week of age when the carcinoma normally is detectable histologically or by ultrasound imaging. The **vaccination with mHER3_FL slowed down tumor progression**

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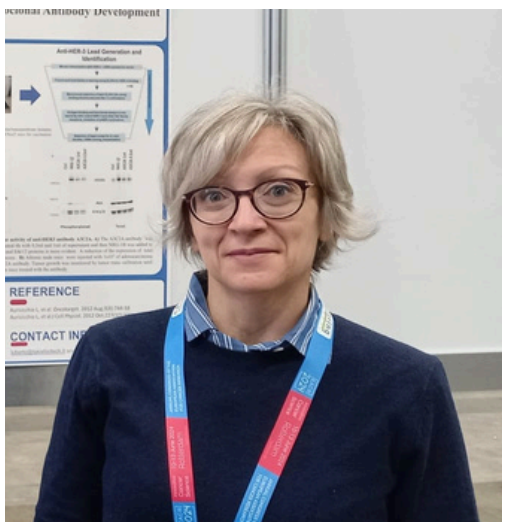
REFERENCES

- Aurisicchio L, et al. Oncotarget. 2012 Aug;3(8):744-58

- Aurisicchio L, et al.J Cell Physiol. 2012 Oct;227(10):3381-8

CONTACTS



Principal Investigator - Takis srl

luberto@takisbiotech.it

Principal Investigator - Takis srl

muzi@takisbiotech.it

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