

## BIO\_02 - Evaluation of antitumor activity of 5 RNA interference in conjunction for the treatment of breast cancer in nude mice

Ana Beatriz Teixeira Frederico<sup>1</sup>; Danielle Regina de Almeida de Brito e Cunha<sup>1</sup>; Tatiana Martins Tilli<sup>2</sup>; Ana Paula Dinis Ano Bom<sup>1</sup>.

<sup>1</sup>Fiocruz/Bio-Manguinhos;

<sup>2</sup>Fiocruz/CDTS.

**Introduction:** Cancer is the second leading cause of death from disease, with breast cancer being the most common and deadliest type of cancer among women worldwide. Only in 2018, breast cancer was responsible for more than 2 million cases worldwide and more than 625,000 people died from the disease. Due to the increase in its incidence, further advances in its treatment are necessary. Therapies using the RNA interference mechanism are in evidence and represent a promising approach to the treatment of breast cancer.

**Objective:** Evaluate the effect of the mixture of 5 siRNA administered intratumorally, at two concentrations, on body weight and tumor progression of human breast carcinoma, using the subcutaneous xenographic tumor model in nude mice.

**Methodology:** Tumor cells from the human breast carcinoma lineage (MDA-MB-231) were implanted on the back of the animals. On the twelfth day after cell implantation, when the tumor presented an approximate volume of 50 mm<sup>3</sup>, the animals were experimentally divided into four groups, so that the groups presented themselves uniformly in terms of tumor volume. The treatments used were: (1) vehicle (PBS); (2) 0.5 mg/kg dose of siRNA mixture, (3) 1 mg/kg dose of siRNA mixture, and (4) 1 mg/kg dose of scrambled siRNA. For *in vivo* siRNA delivery, InvivoFectamine was used as a reagent of transfection. Administrations were performed on days 15, 21 and 28 of the study by the intratumoral route. Animals were reported daily for morbidity and mortality. The tumor volume and body weight of the animals were analyzed every three days until the 39th of the study.

**Results:** The “vehicle” group present a tumor volume of 249.8 ± 64.08 mm<sup>3</sup> at the end of the 39th day of the study, an increase in tumor size of approximately 3.8 times when compared to the first day of treatment. Treatment with siRNAs at doses of 0.5 mg/kg and 1 mg/kg prevented tumor growth over the 24th day after the start of treatments. On the last day of treatment, a smaller tumor volume was observed than was observed on the first day of treatment, these groups had a tumor volume of 21.41 ± 9.67 mm<sup>3</sup> and 18.63 ± 9.26 mm<sup>3</sup> for the doses of 0.5 mg/kg and 1 mg/kg, respectively. Finally, scramble siRNA administered at a dose of 1 mg/kg showed a slight reduction in tumor growth over the 24 days after the start of treatments.

**Conclusion:** The results of this work demonstrated that the mixture of the 5 siRNA was effective in inhibiting tumor growth in the xenographic subcutaneous tumor model of human breast carcinoma in nude mice, at both doses used.

**Keywords:** RNA interference; siRNA; Breast cancer