

A new model of tumorigenesis and axons regulation for the pancreatic cancer

Marie-José CHAAYA, I2M - Marseille

Sophie CHAUVET, IBDM - Marseille

Florence HUBERT, I2M - Marseille

Fanny MANN, IBDM - Marseille

Mathieu MÉZACHE, INRAE - Jouy-en-Josas

Pancreatic cancer is a cancer with a very low life expectancy. The most known type of pancreatic cancer happens in the cells that line the ducts that carry digestive enzymes out of the pancreas called pancreatic ductal adenocarcinoma (PDAC). Studies has been made on this not-so-easy cancer in order to better understand how to approach this disease. Through recent studies, it was shown that the neuron cells of the peripheral nervous system innervate the tumor microenvironment and play a significant role in the regulation of PDAC cancer. However, the relationship between cancer development and its interaction with the peripheral nervous system is still not very clear. According to [5, 3], it is now well established that the nervous system impacts the tumor progression, but the relationship between tumor progression and the nervous system is still poorly understood and is likely to involve a multitude of factors.

One example of question that remains to be investigated is the role of sympathetic neurons on the initiation and progression of PDAC. Two contradictory results were given by [5] that states that sympathetic neurons have a pro-tumoral effect and by [3] that states that sympathetic neurons have an anti-tumoral effect and that the pro-tumoral effect is due to the remodelling of sensory axons in the PDAC.

It is therefore relevant to study tumor-nerve interactions through mathematical modelling to better understand this problem.

The main goal of this talk is then to present a new continuous mathematical model of PDAC cancer growth and its interaction with the peripheral nervous system in the lights of the recent works in the literature of [2], [4], and [1]. In silico denervation experiments will be proposed to better understand the contradictory results of [5, 3].

- [1] S. Chauvet, F. Hubert, F. Mann, M. Mezache. *Tumorigenesis and axons regulation for the pancreatic cancer : a mathematical approach*. Journal of Theoretical Biology, **556**, 111301, 2023.
- [2] R. Eftimie, L. Gibelli. *A kinetic theory approach for modelling tumour and macrophages heterogeneity and plasticity during cancer progression*. Mathematical Models and Methods in Applied Sciences, **30(04)**, 659–683, 2020.
- [3] J. Guillot, C. Dominici, A. Lucchesi, T. T. H. Nguyen, J. Nigri, F. Guillaumond, M. Bigonnet, N. Dusetti, A. Etzerodt, T. Lawrence, P. Pudlo, F. Hubert, J.-Y. Scoazec, S. A. van de Pavert, R. Tomasini, S. Chauvet, F. Mann. *Sympathetic axonal sprouting induces changes in macrophage populations and protects against pancreatic cancer*. to appear, 2022.
- [4] G. Lolas, A. Bianchi, K. N. Syrigos. *Tumour-induced neurogenesis and perineural tumour growth : a mathematical approach*. Scientific reports, **6(1)**, 1–10, 2016.
- [5] B. W. Renz, R. Takahashi, T. Tanaka, M. Macchini, Y. Hayakawa, Z. Dantes, H. C. Maurer, X. Chen, Z. Jiang, C. B. Westphalen, et al. *$\beta 2$ adrenergic-neurotrophin feedforward loop promotes pancreatic cancer*. Cancer cell, **33(1)**, 75–90, 2018.