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# VENOM PEPTIDES: EMERGENT BIOLOGICAL TOOLS FOR LUNG CANCER IMAGING

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Many cancers, including non-small cell lung cancer (NSCLC), are associated with disrupted mechanisms due to dysfunction and/or overexpression of numerous ion channels such as certain subtypes of sodium ( $\text{Na}_v1.7$ ) and potassium ( $\text{K}_{Ca3.1}$ ) channels, ASICs (acid sensing ion channels) or nicotinic acetylcholine receptors ( $\alpha7$ ,  $\alpha9/\alpha10$ ). In particular, the activation of these ion channels plays an important role in cancer cell aggressiveness and tumor invasion<sup>1</sup>, their overexpression seeming to be correlated with the appearance of metastases. Although imaging approaches (radiography, CT-scan for computed tomography scanning, PET-scan for positron emission tomography) are commonly used in the anatomical characterization of NSCLC, some limitations require the development of new imaging probes more specific of overexpressed molecular targets lung adenocarcinomas<sup>2</sup>. Peptide toxins are known to act selectively and with high affinity on certain ion channels overexpressed in cancer cells. The development of new imaging agents for NSCLC will therefore involve exploiting the pharmacological properties of peptide toxins, and will focus on three research areas : (1) the chemical synthesis of these toxins enabling them to be labelled by "click" chemistry, using fluorescent or radioactive probes, (2) the functional validation of labelled toxins using electrophysiological techniques to ensure that their pharmacological properties are maintained, and (3) proof-of-concept through *in vitro* imaging of adenocarcinoma lines and *in vivo* imaging of xenografted mice to validate the specificity and quality of labelled toxins. Mambalgine, an ASIC-targeted toxin, was synthesized with and without fluorochrome. The overexpression of  $\text{Na}_v1.7$ ,  $\alpha7$  and  $\alpha9$  proteins in lung cancer cell lines was validated. In addition, their membrane expression was also validated by fluorescence microscopy, using the tagged toxins. These preliminary results are highly encouraging for designing the "labeled toxin/ion channel" pair as an imaging tool to detect NSCLC.

## References:

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