

#### Venom peptides: emerging biological tools for lung cancer diagnosis

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# Venom peptides: promising tools for lung cancer diagnosis



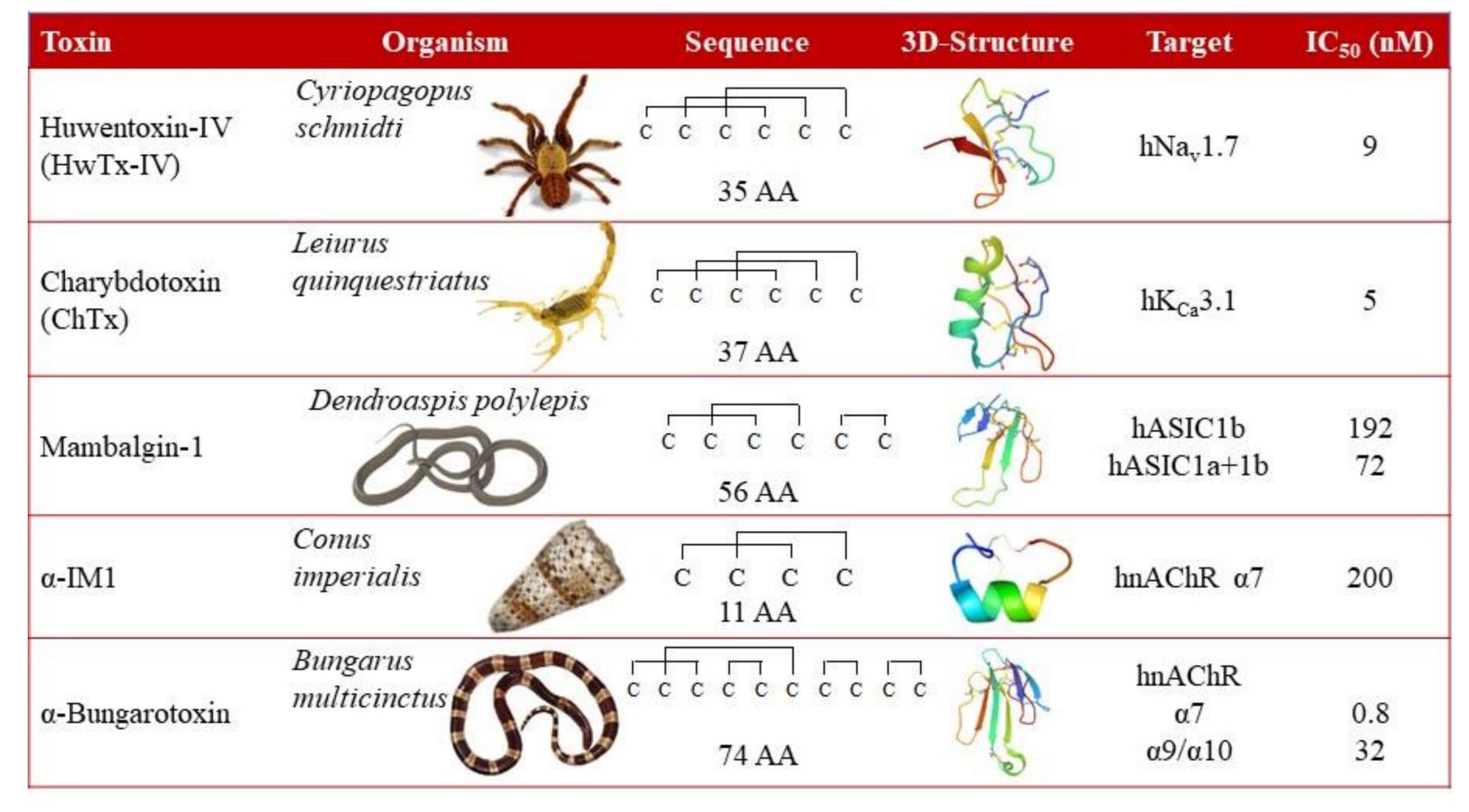
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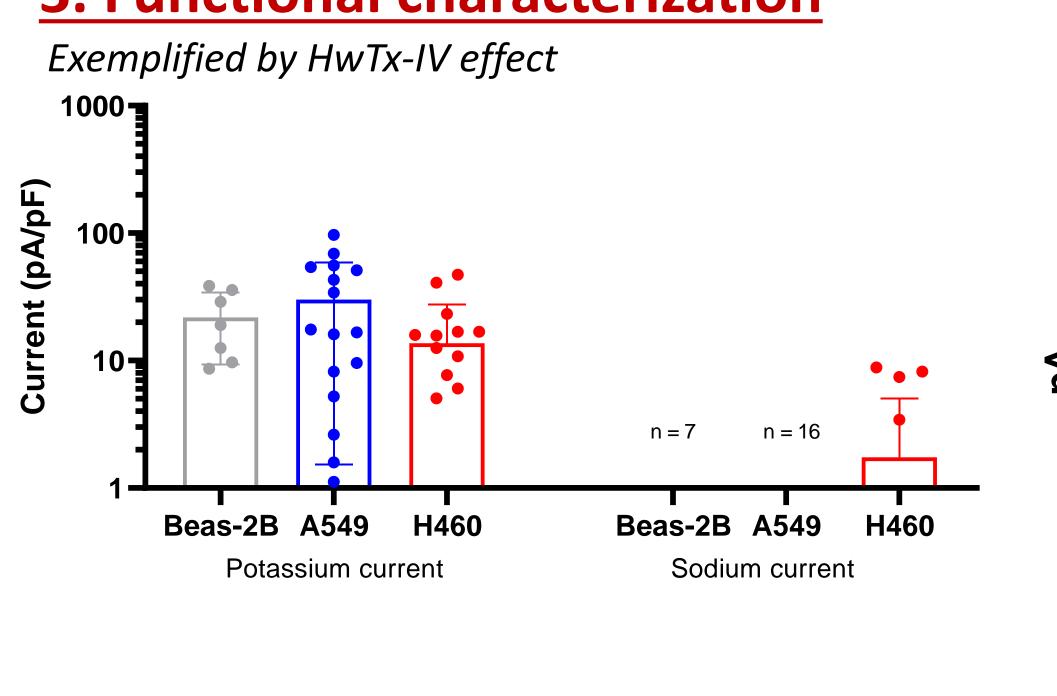
Many cancers, and the non-small cell lung cancer (NSCLC) in particular, are associated with significant overexpression of various ion channels such as certain subtypes of sodium, calcium and potassium channels, pH-sensitive channels (ASICs for acid sensing ion channels) or nicotinic acetylcholine receptors. Activation of these ion channels plays an important role in the aggressiveness of cancer cell and tumor invasion, 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 lung cancer, some limitations of these approaches require the development of new imaging probes more specific of overexpressed molecular targets in lung adenocarcinomas. Peptide toxins, which possess unique pharmacological properties, are well known to act selectively and with high affinity on certain overexpressed ion channels in cancer cells. Therefore, a promising solution towards the development of new imaging agents of lung cancer biomarkers appears to be the chemical synthesis of these toxins allowing them to be labelled by "click" chemistry using various fluorescent or radioactive probes.

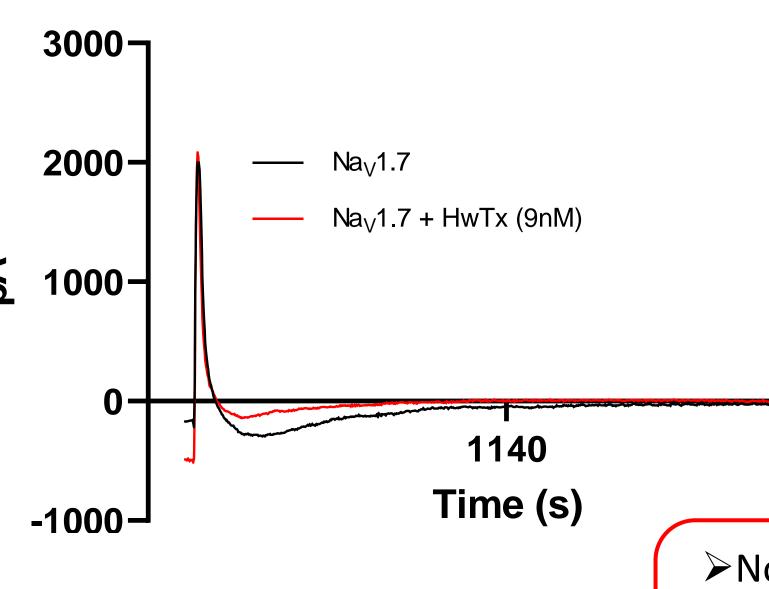
### 1. Peptide synthesis



#### All peptides are synthetised by Solid-Phase Peptide Synthesis (SPPS)

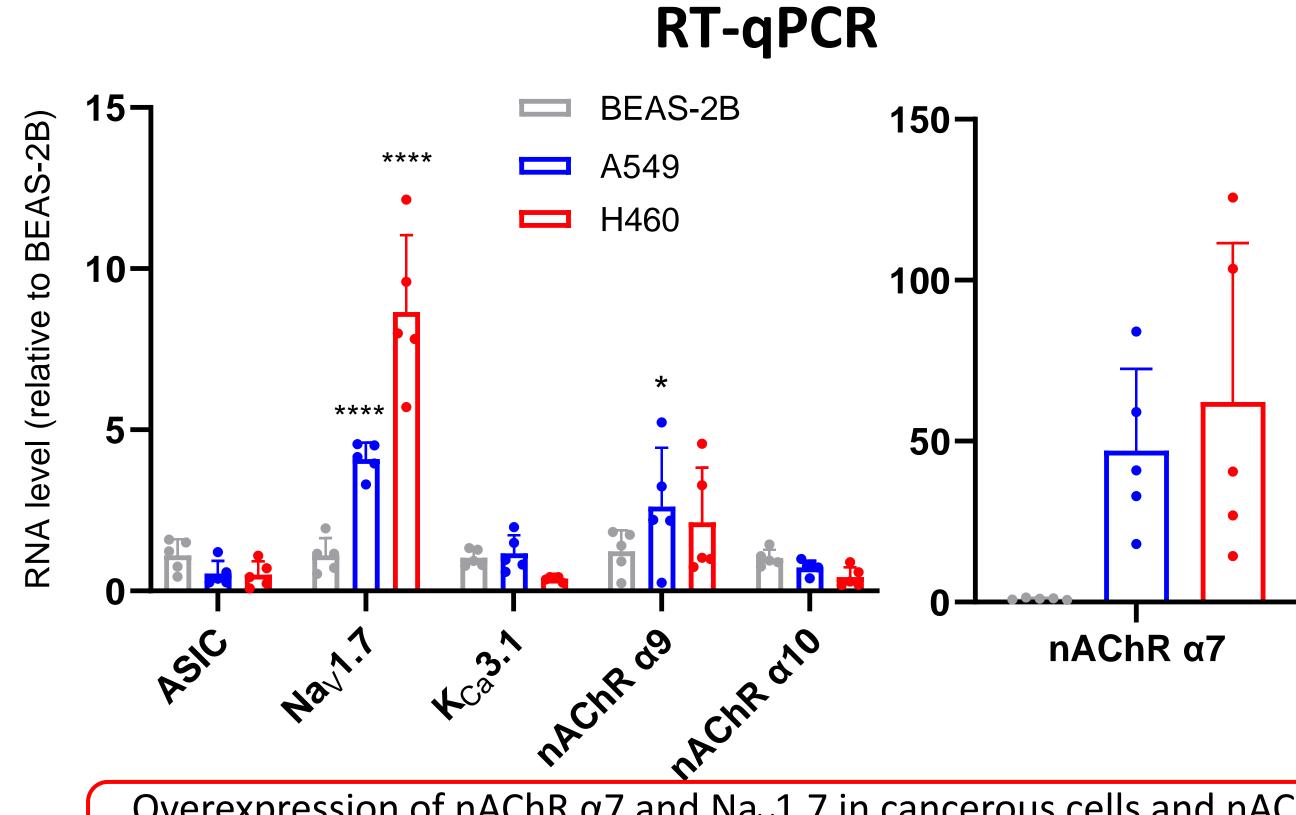
## 3. Functional characterization



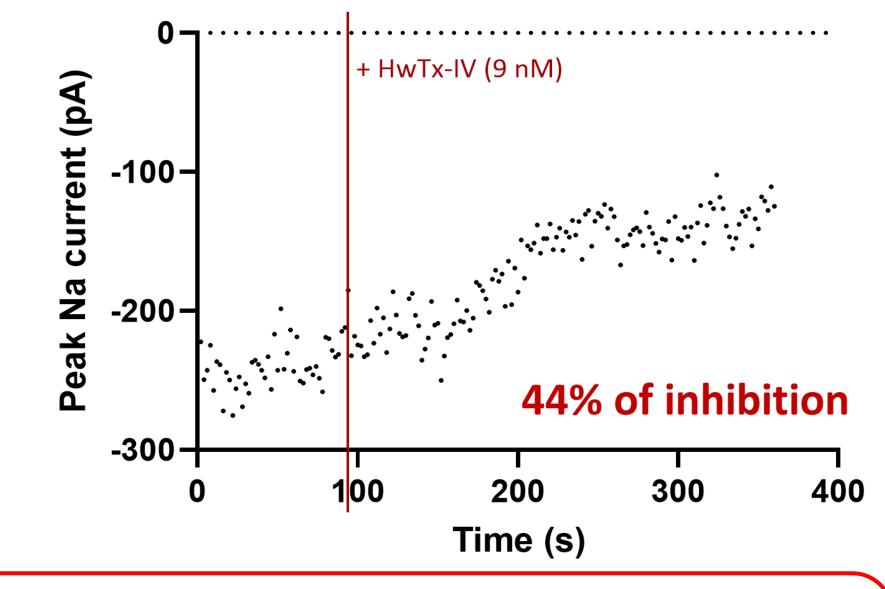


# 2. Gene expression

Cell lines Beas-2B Non cancerous cell line Cancerous cell line H460 Cancerous and strongly metastatic cell line



Overexpression of nAChR  $\alpha$ 7 and Na $_{\rm V}$ 1.7 in cancerous cells and nAChR α9 only in A549 cells

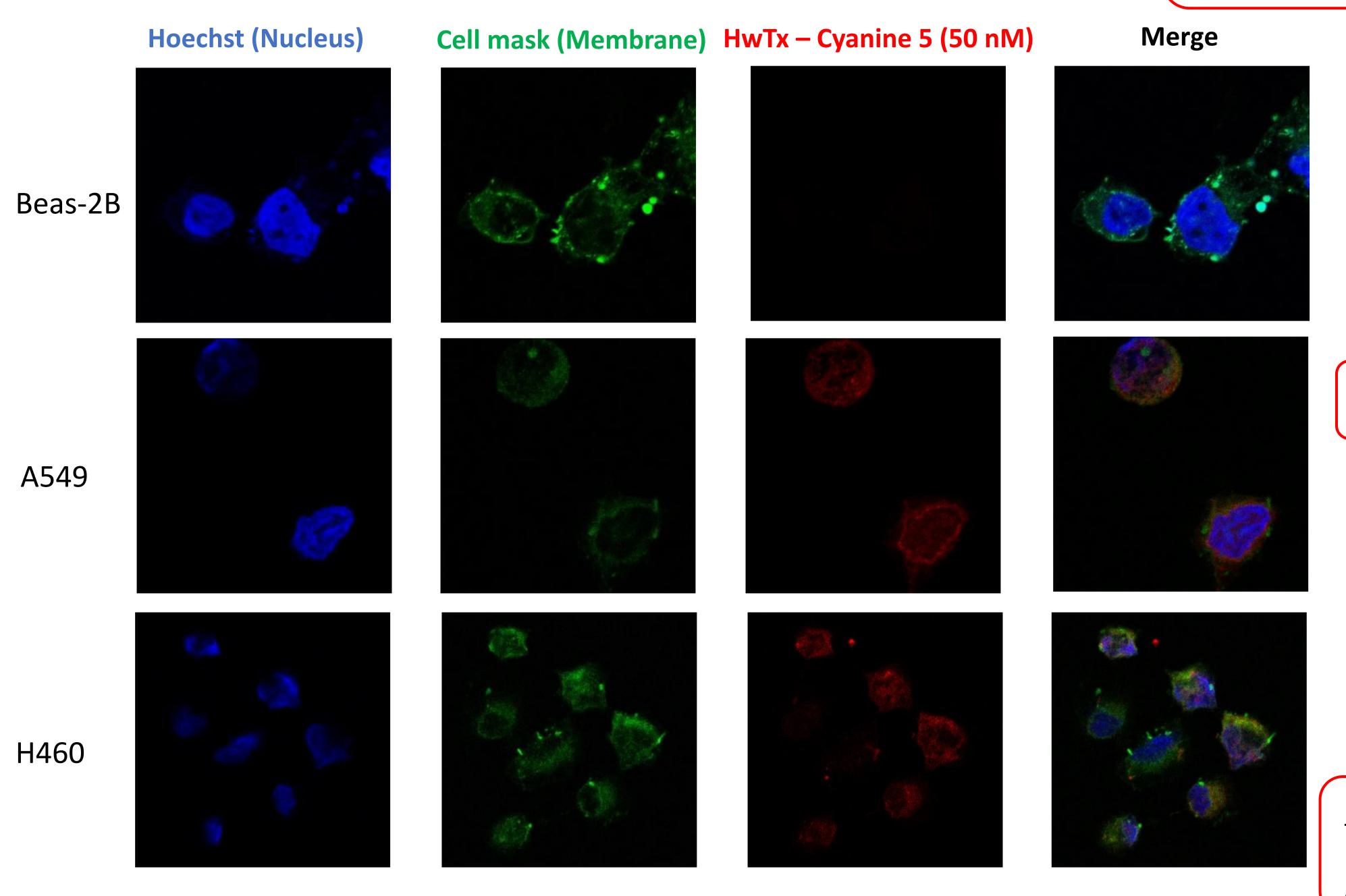


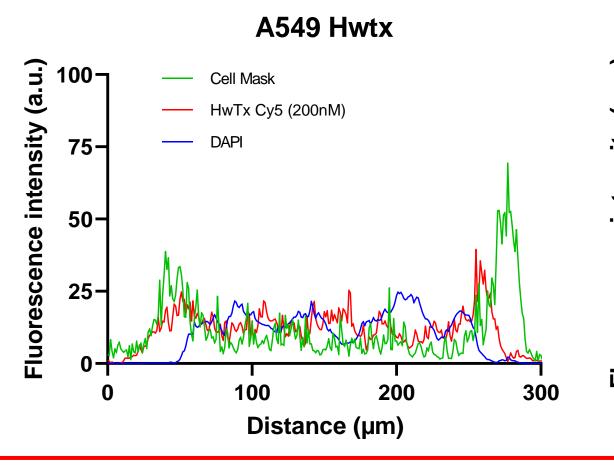
- ➤ No detectable sodium current in Beas-2B and A549 cells
- > Weak sodium current in H460 (unexploitable for HwTx-IV studies)
- $\rightarrow$  Use of HEK-293 cell line stably overexpressing hNa<sub>V</sub>1.7
- → Experiments with HwTx-IV-Cyanine 5

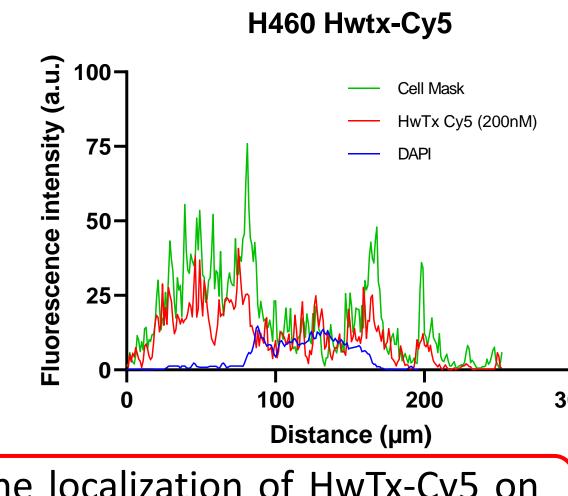
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# 4. Fluorescence imaging

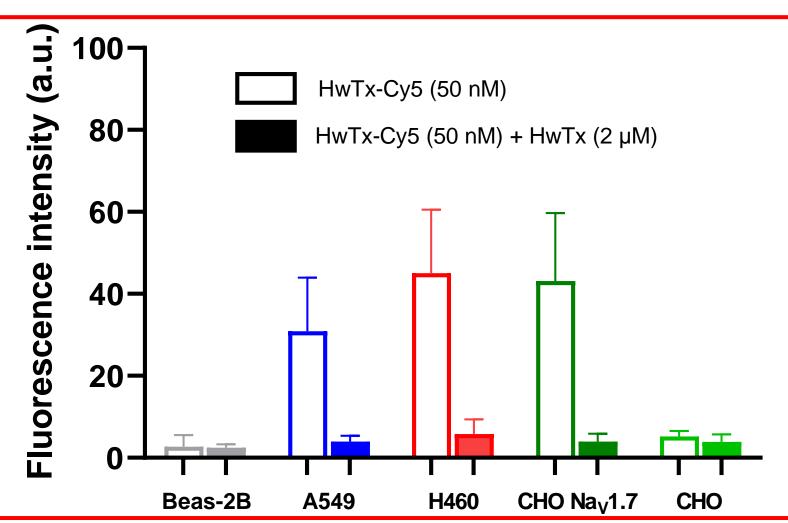
Exemplified by HwTx-IV-Cyanine 5 effect on lung cell lines







Profil of fluorescence showing the localization of HwTx-Cy5 on the membrane of cancerous cell lines.



HwTx-IV-Cy5 interacts with Na<sub>v</sub>1.7 channels. Noted that the fluorescence intensity is significantly higher in cancerous than Beas-2B cells. Excess of unlabbeled toxins markedly decrease the signal indicating the specificity of interactions.

Certain ionic channels are overexpressed in lung cancer cell lines. These channels can be targetted with high affinity and selectivity by some venom toxins that are easily tagged with fluorescent or radioactive group. The results show that the Na $_{
m V}$ 1.7 and HwTx-IV-Cyanine 5 couple is promising to detect tumors, especially invasive ones. To complete these results, TEP imaging will be done on xenografted mice. This study will participate to the development of new lung cancer biomarkers