# Pronounced peptide selectivity for melanoma through tryptophan end-tagging

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Effects of oligotryptophan end-tagging on the uptake of arginine-rich peptides into melanoma cells was investigated under various conditions and compared to that into non-malignant keratinocytes, fibroblasts, and erythrocytes, also monitoring resulting cell toxicity. In parallel, biophysical studies on peptide binding to, and destabilization of, model lipid membranes provided mechanistic insight into the origin of the selectivity between melanoma and non-malignant cells. Collectively, the results demonstrate that W-tagging represents a powerful way to increase selective peptide internalization in melanoma cells, resulting in toxicity against these, but not against the non-malignant cells. These effects were shown to be due to increased peptide adsorption to the outer membrane in melanoma cells, caused by the presence of anionic lipids such as phosphatidylserine and ganglioside GM1, and to peptide effects on mitochondria membranes and resulting apoptosis. In addition, the possibility of using W-tagged peptides for targeted uptake of nanoparticles/drug carriers in melanoma was demonstrated, as was the possibility to open up the outer membrane of melanoma cells in order to facilitate uptake of low Mw anticancer drugs, here demonstrated for doxorubicin.