

Vismodegib-loaded nanoformulation for topical skin cancer therapy: reducing drug amounts while reaching supra- therapeutic concentrations

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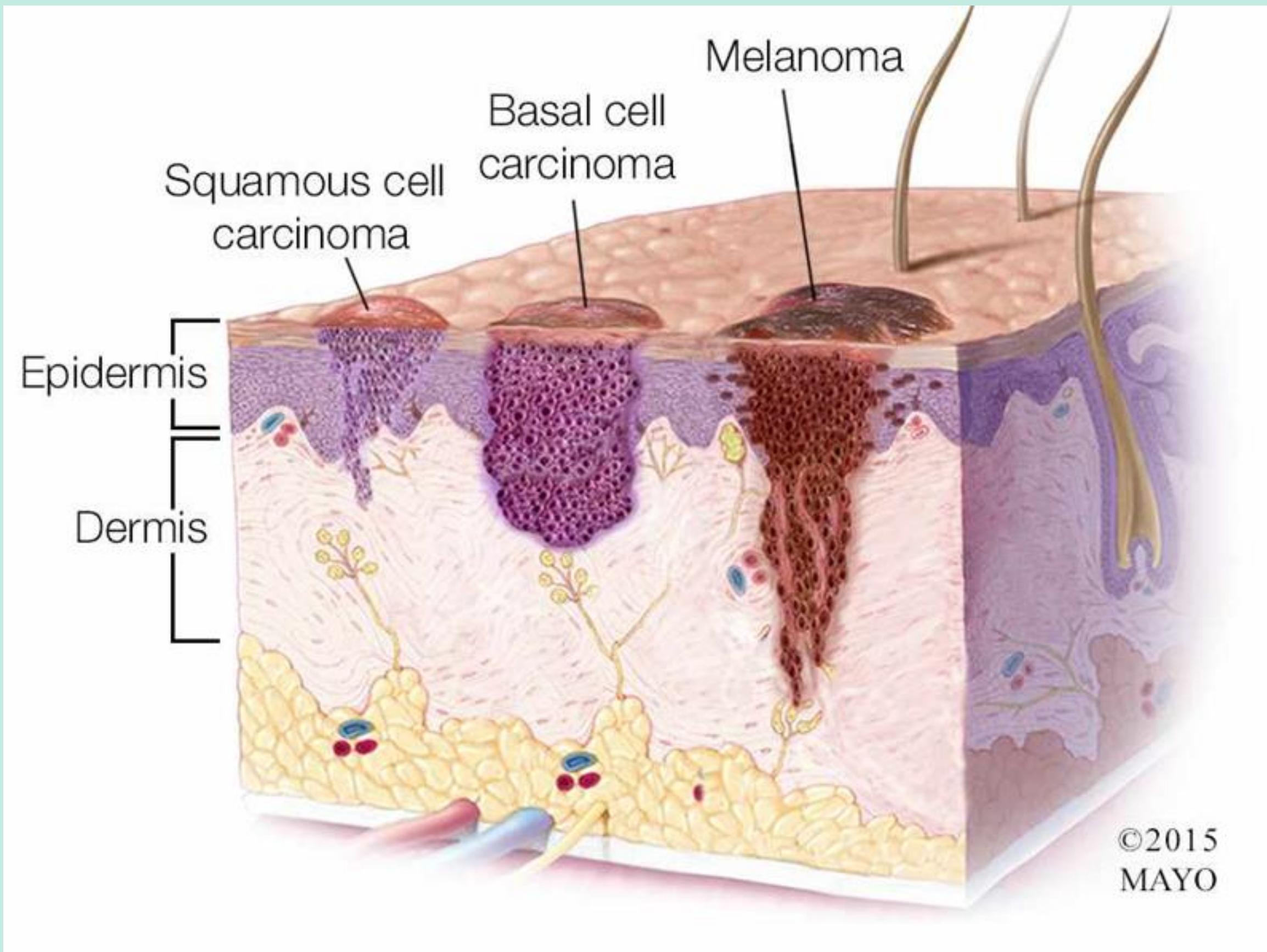
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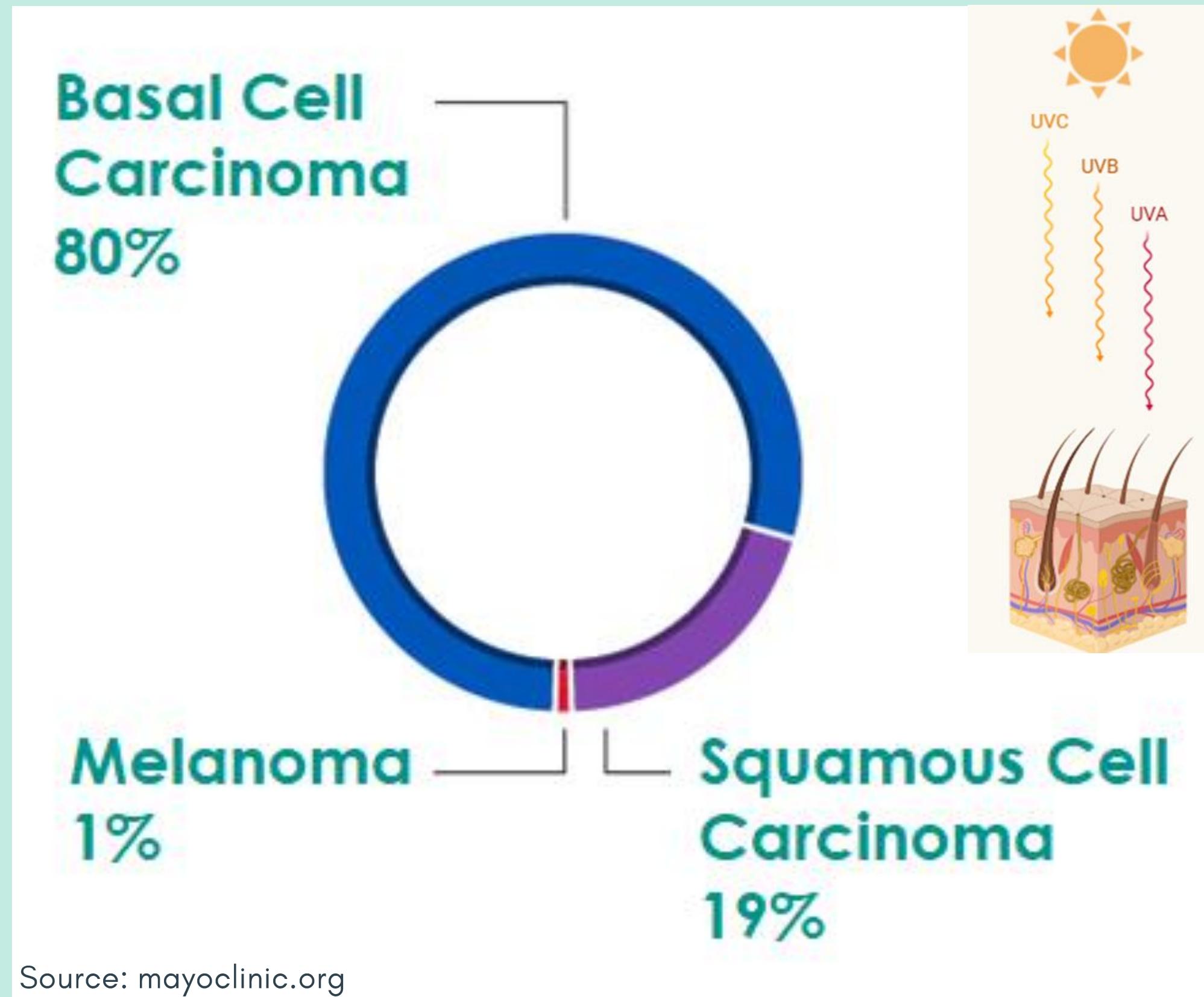
SKIN CANCER

Not all skin cancers are the same



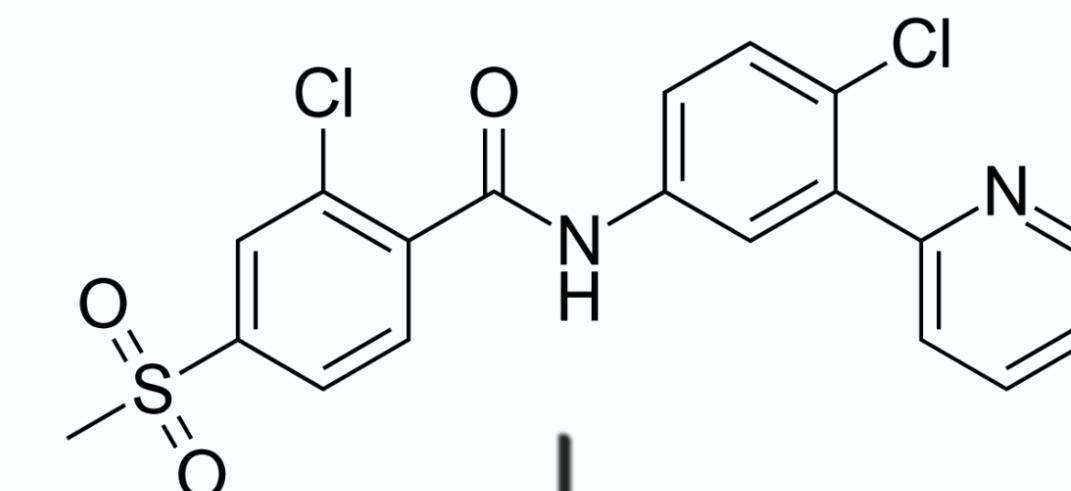
SKIN CANCER

More fun, less sun

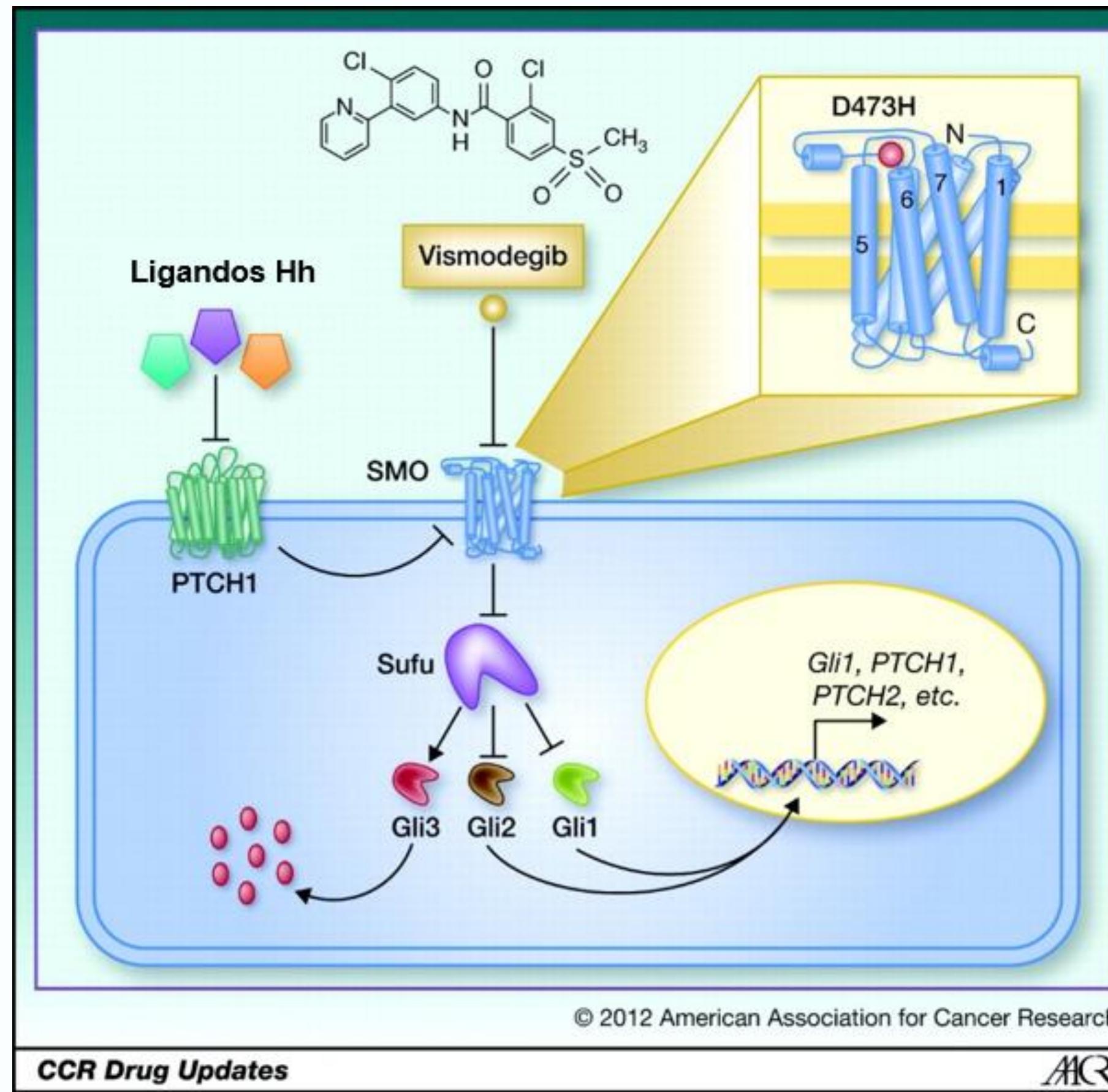


90% of skin cancers are linked to sun exposure





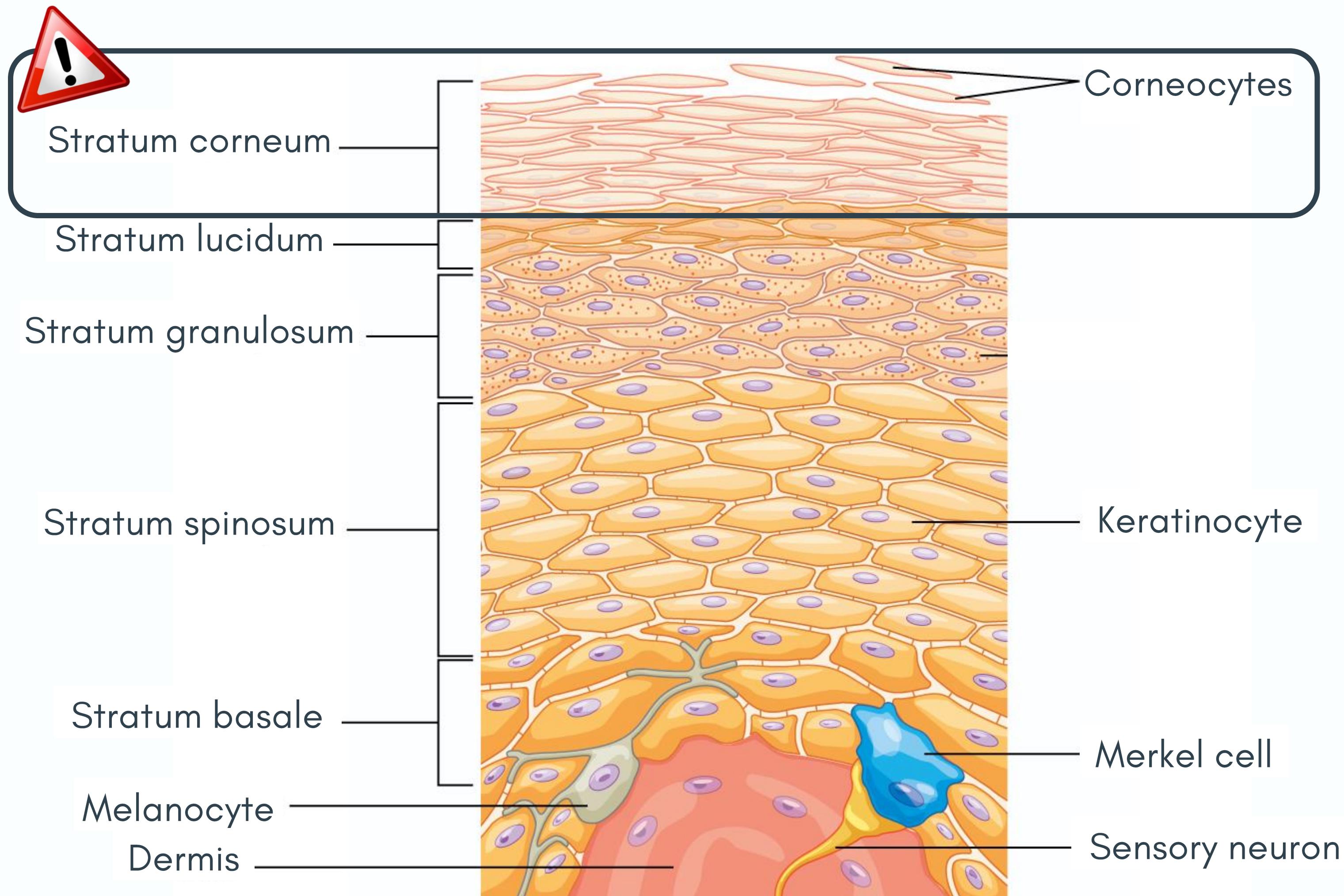
Hedgehog signaling pathway



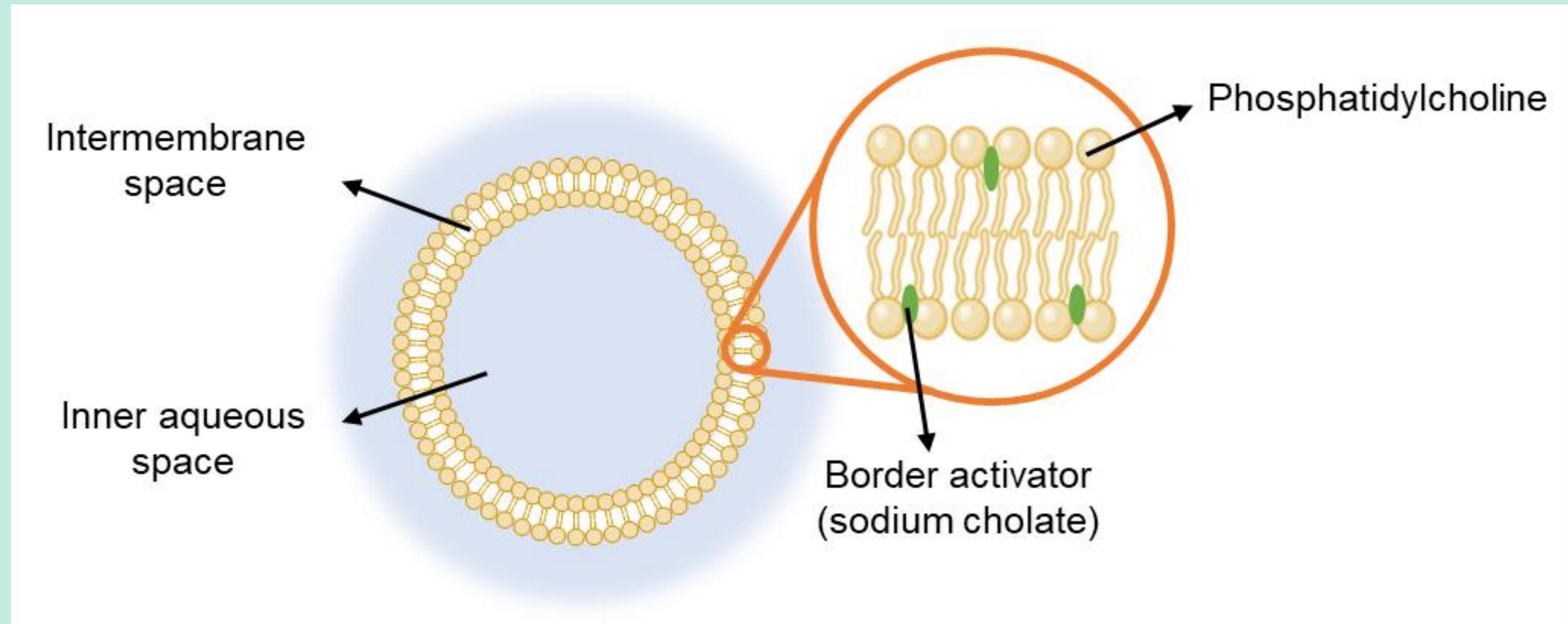
Aim

- To develop a local and site-specific treatment with Vismodegib against Basal Cell Carcinoma using a nano-drug delivery system
- To change the administration pathway of Vismodegib, from oral to topical, in order to reduce side effects in health tissues and organs

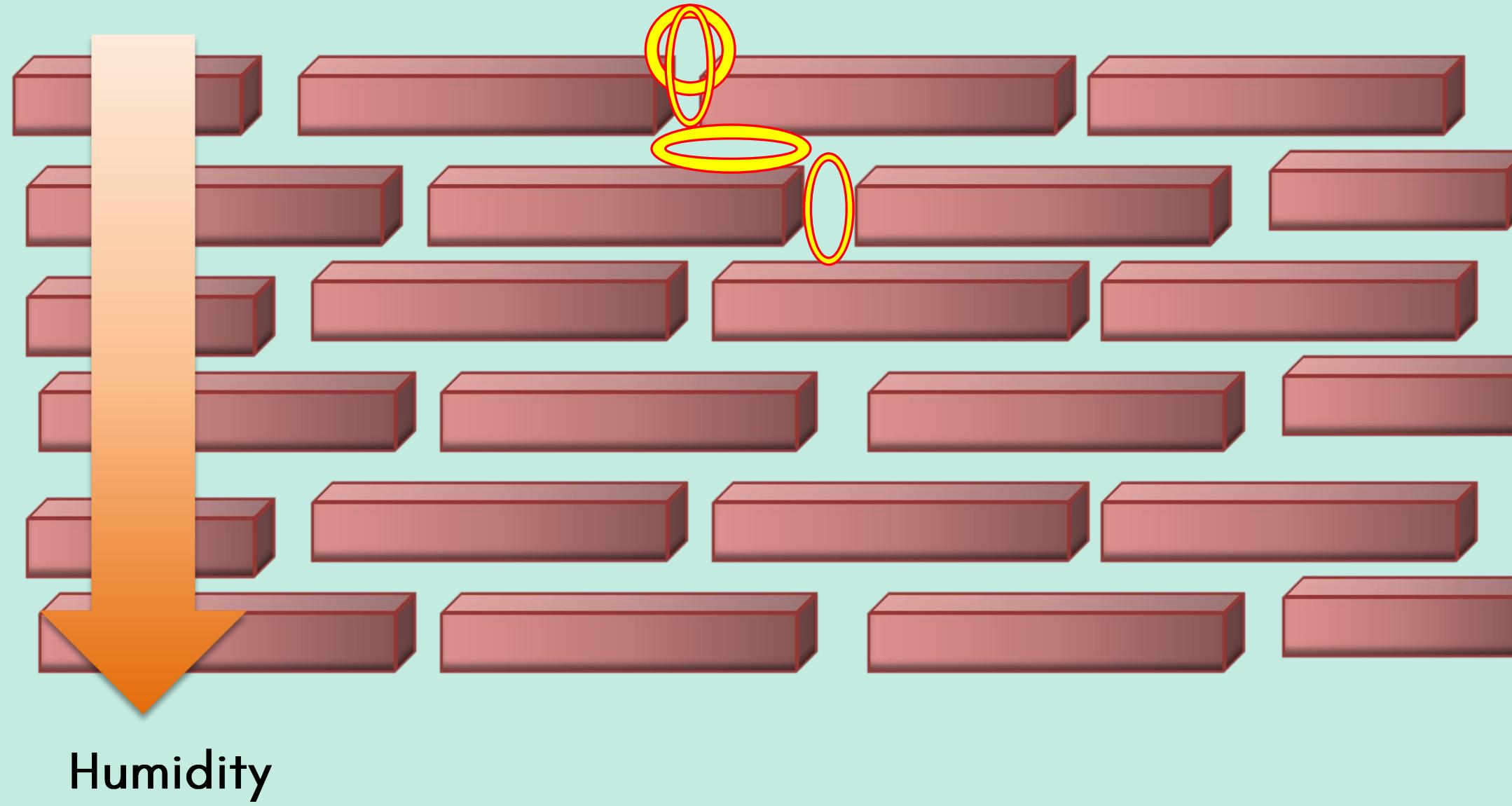
HEALTHY SKIN



Ultradeformable liposomes (UDL)

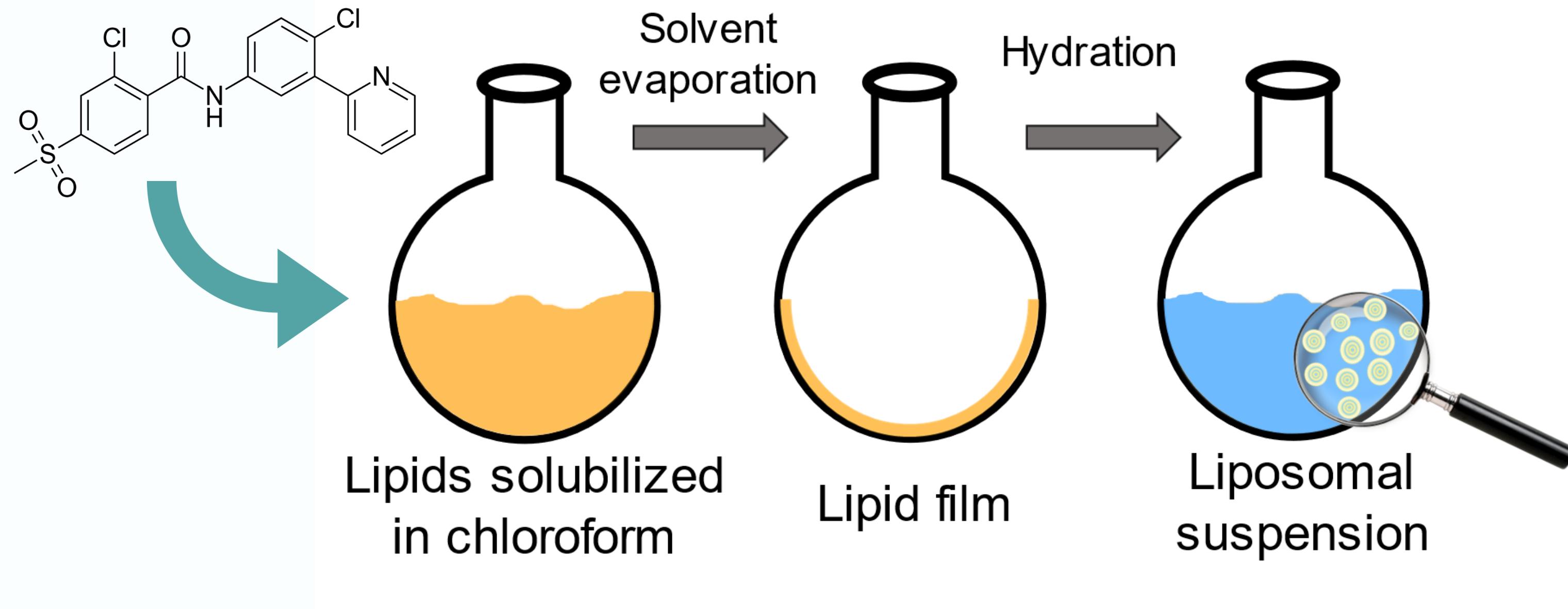


Ultradeformable liposomes (UDL)



UDL are capable of passing through the stratum corneum of the skin
enabling the transport of actives by topical administration

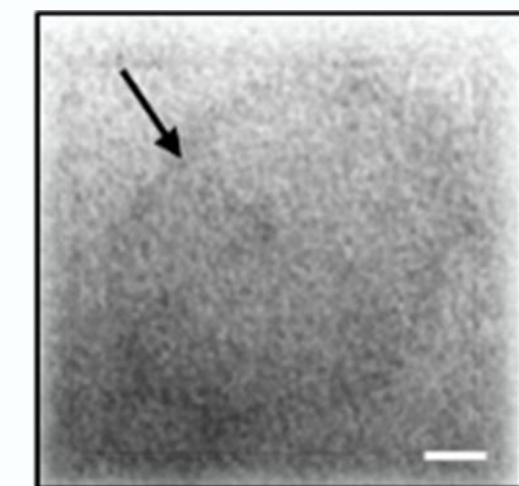
UDL loaded with Vismodegib



Calianni et al., (2019). Nanoformulation for potential topical delivery of Vismodegib in skin cancer treatment. International journal of pharmaceutics, 565, 108-122.

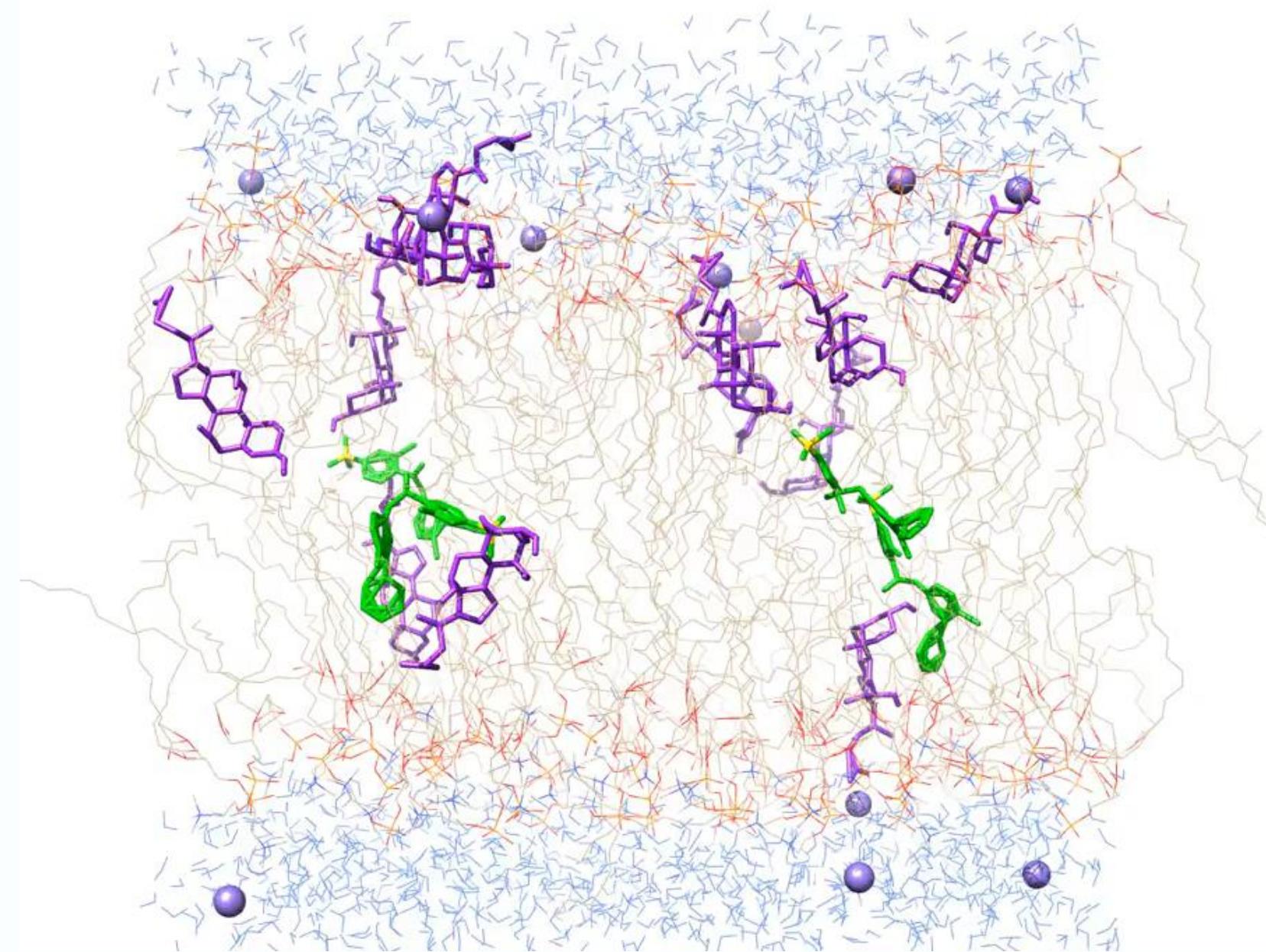
Physicochemical characterization

- ✓ UDL-Vis of around 110 nm in average size and negative Zeta potential ($-18 \pm 1 \text{ mV}$) were obtained
- ✓ No significant changes in the average size and Zeta potential were observed during 30 days of storage at 4°C
- ✓ The encapsulation efficiency was $91.98 \pm 5.14\%$



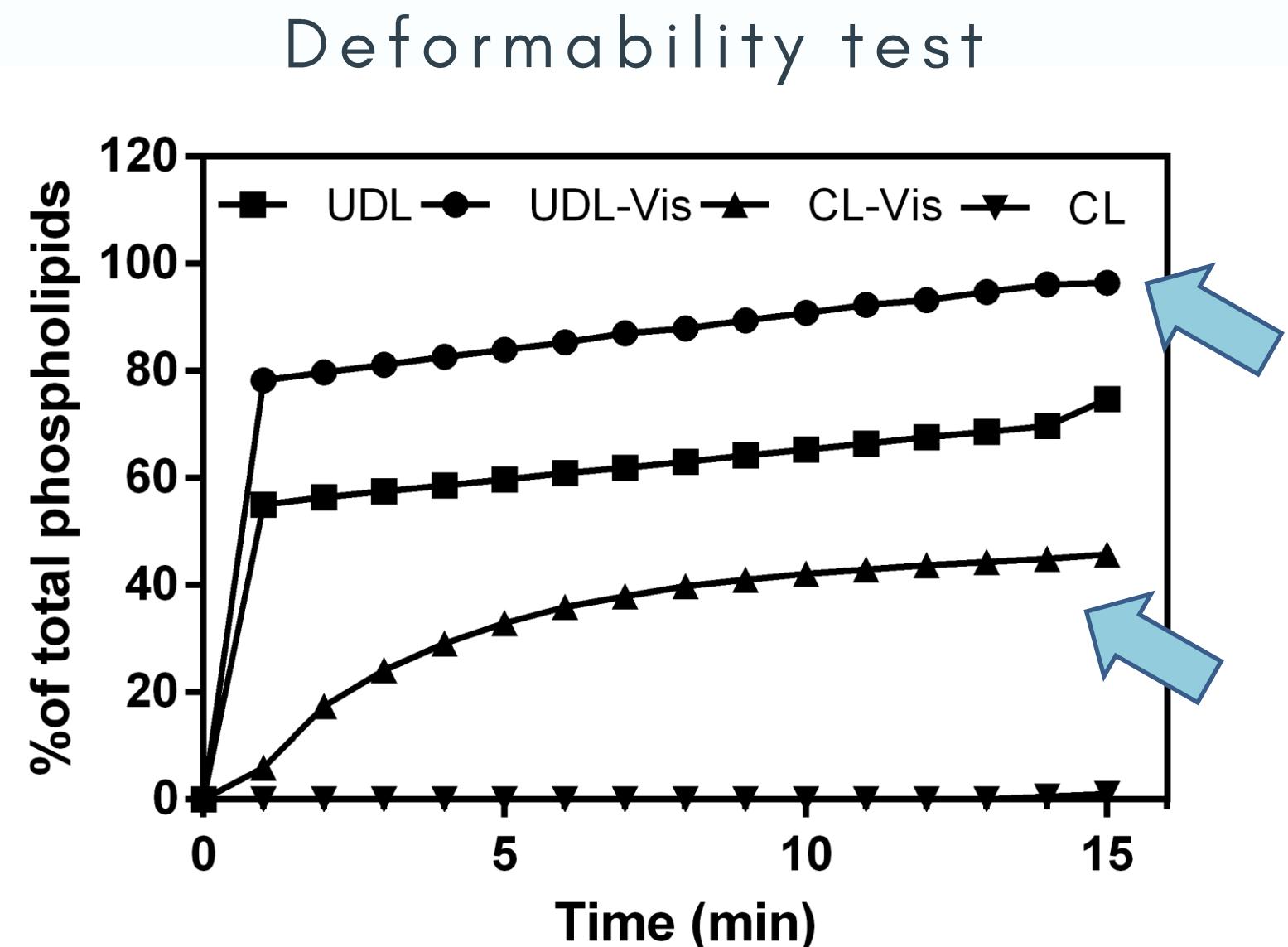
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Physicochemical characterization



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Physicochemical characterization

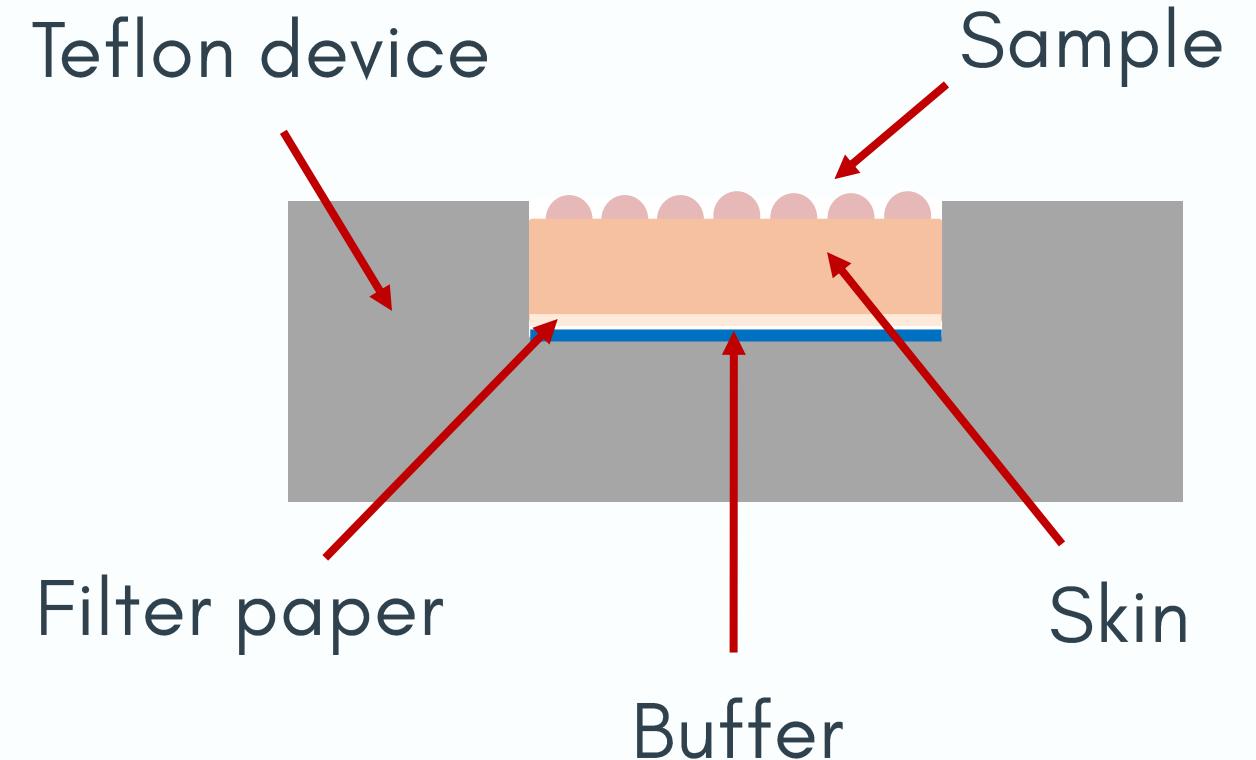
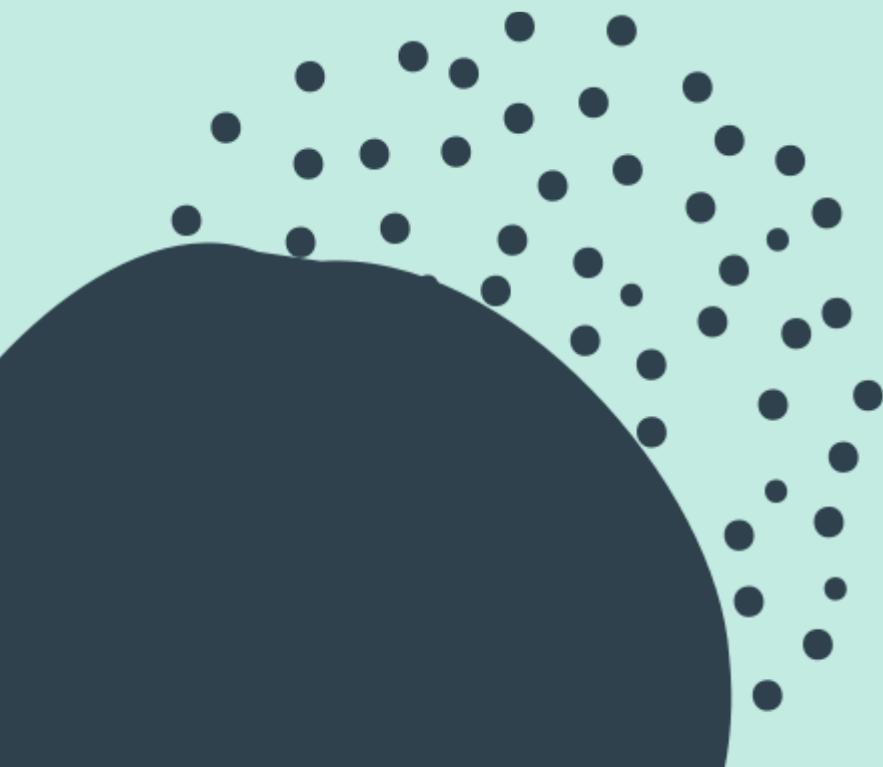


Sample	$D = J (r_v/r_p)^2$
UDL	4419
UDL-Vis	6152
CL-Vis	2447
CL	5

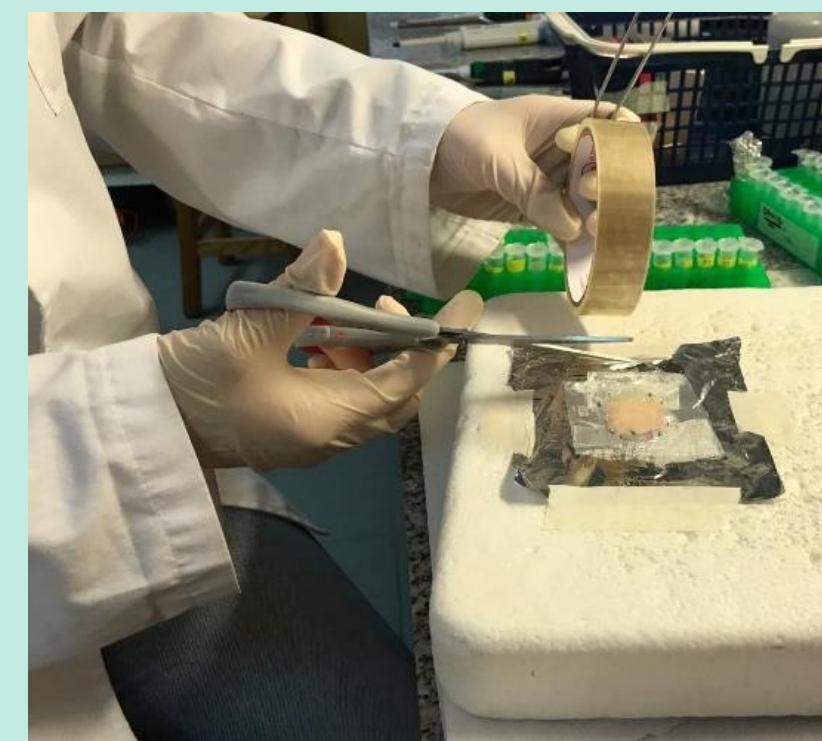
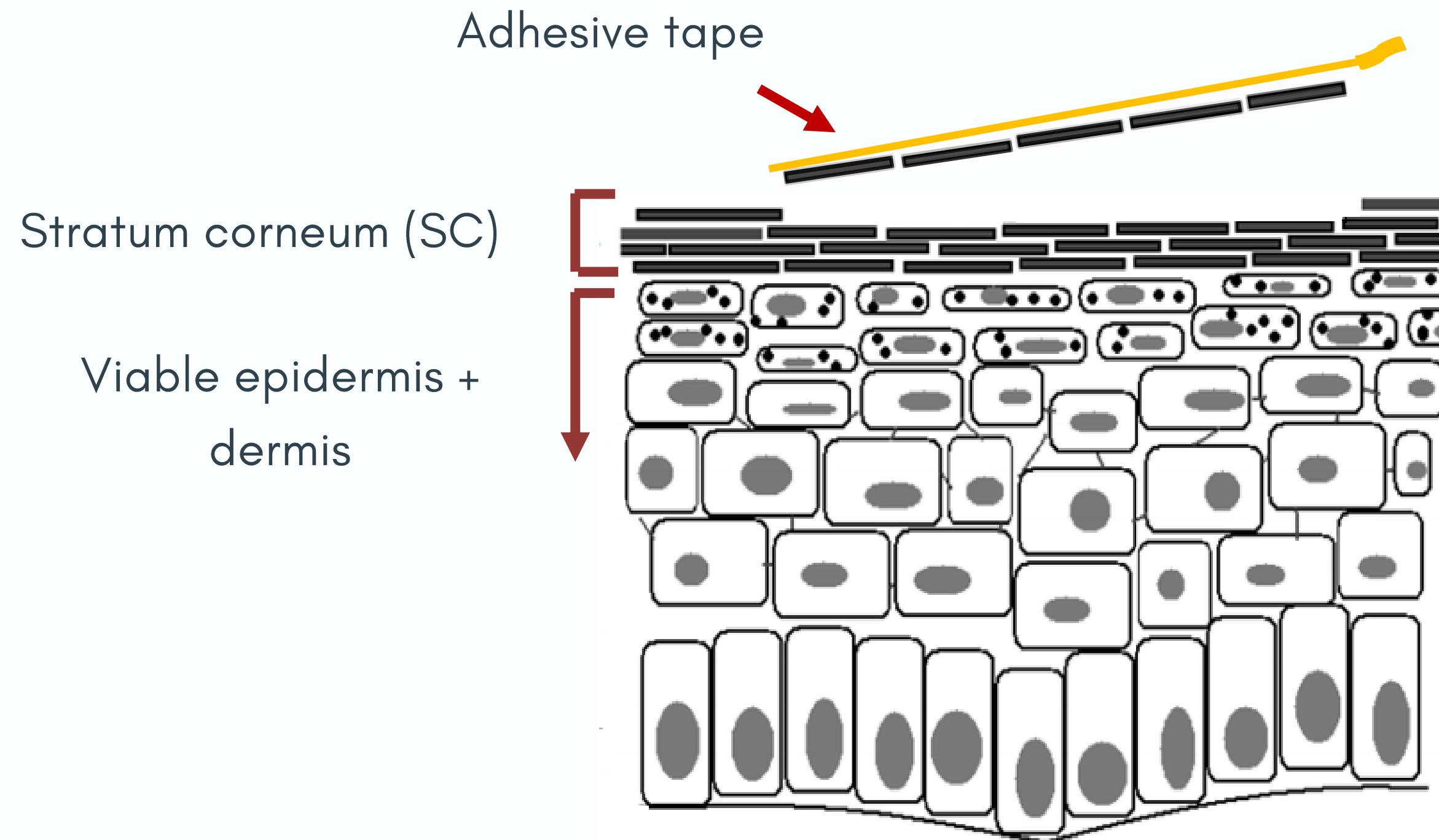
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Skin penetration studies

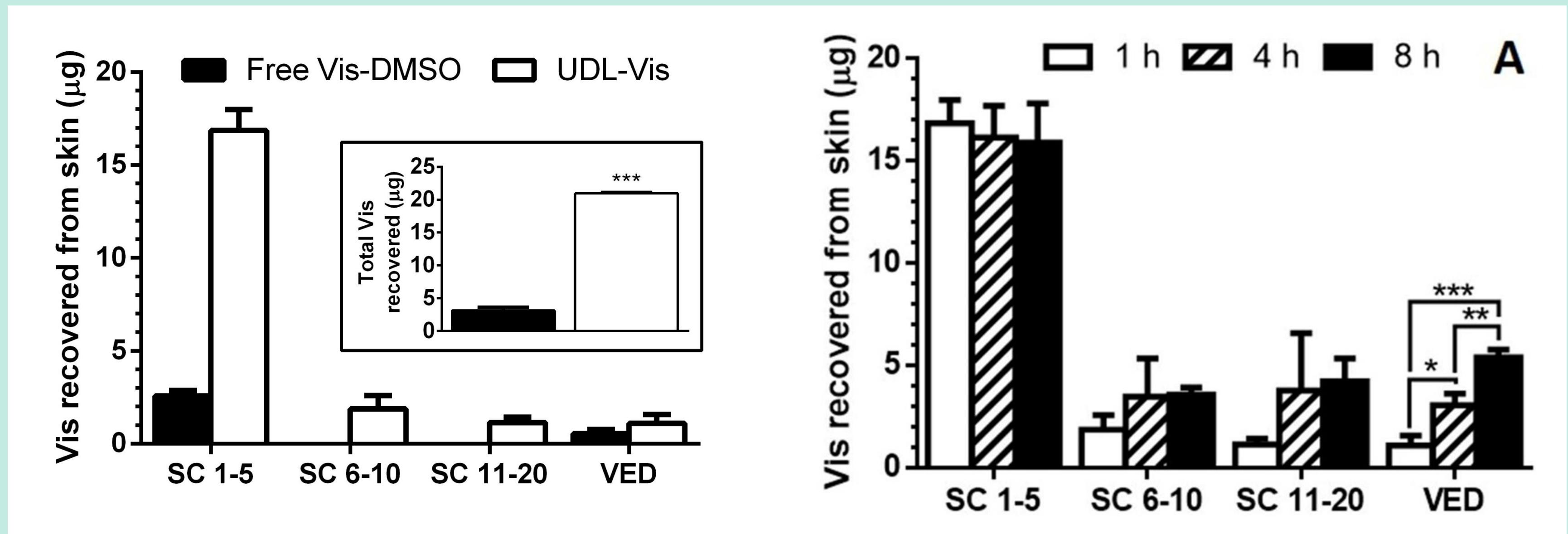
Saarbrücken Penetration Model



Tape stripping

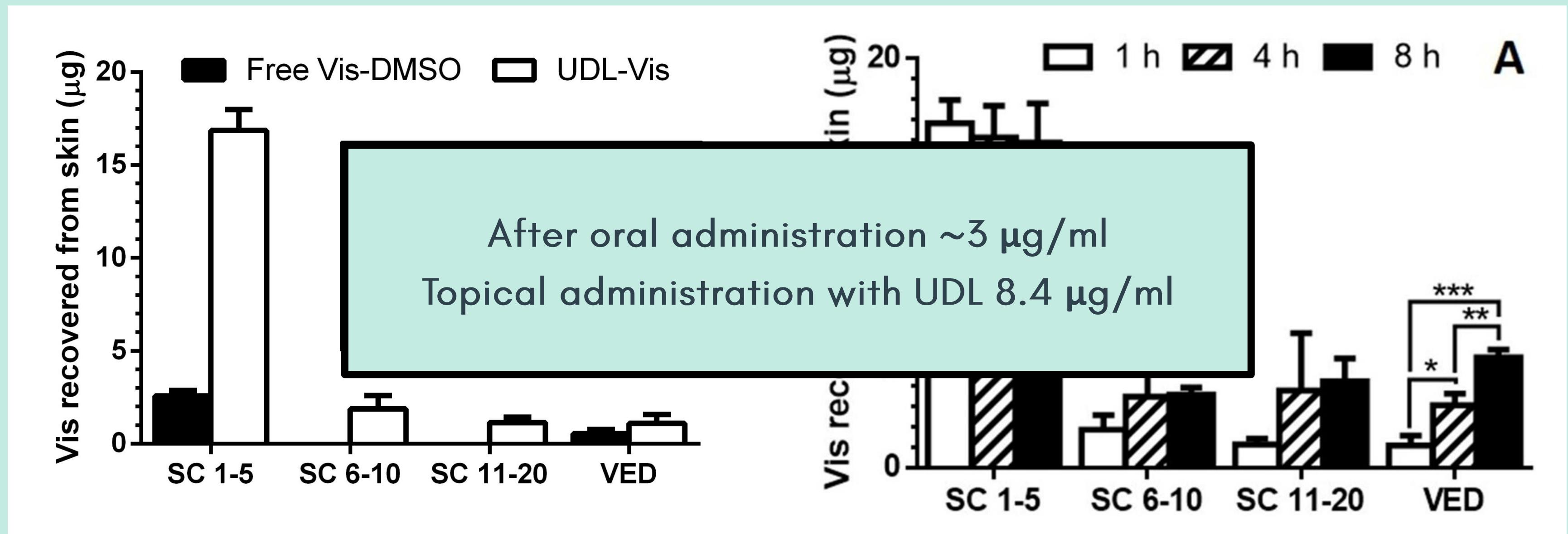


Skin penetration



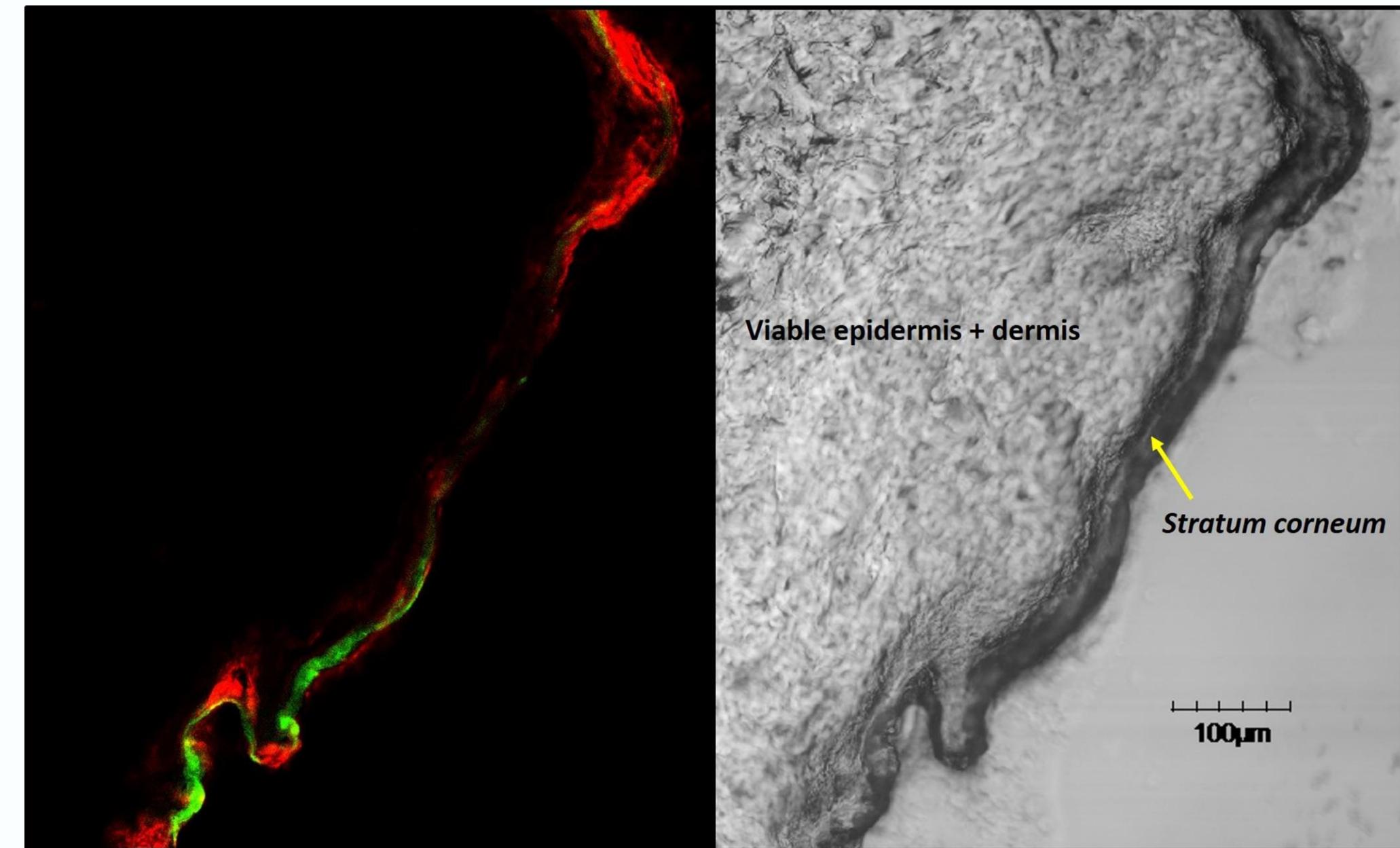
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Skin penetration



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skin penetration



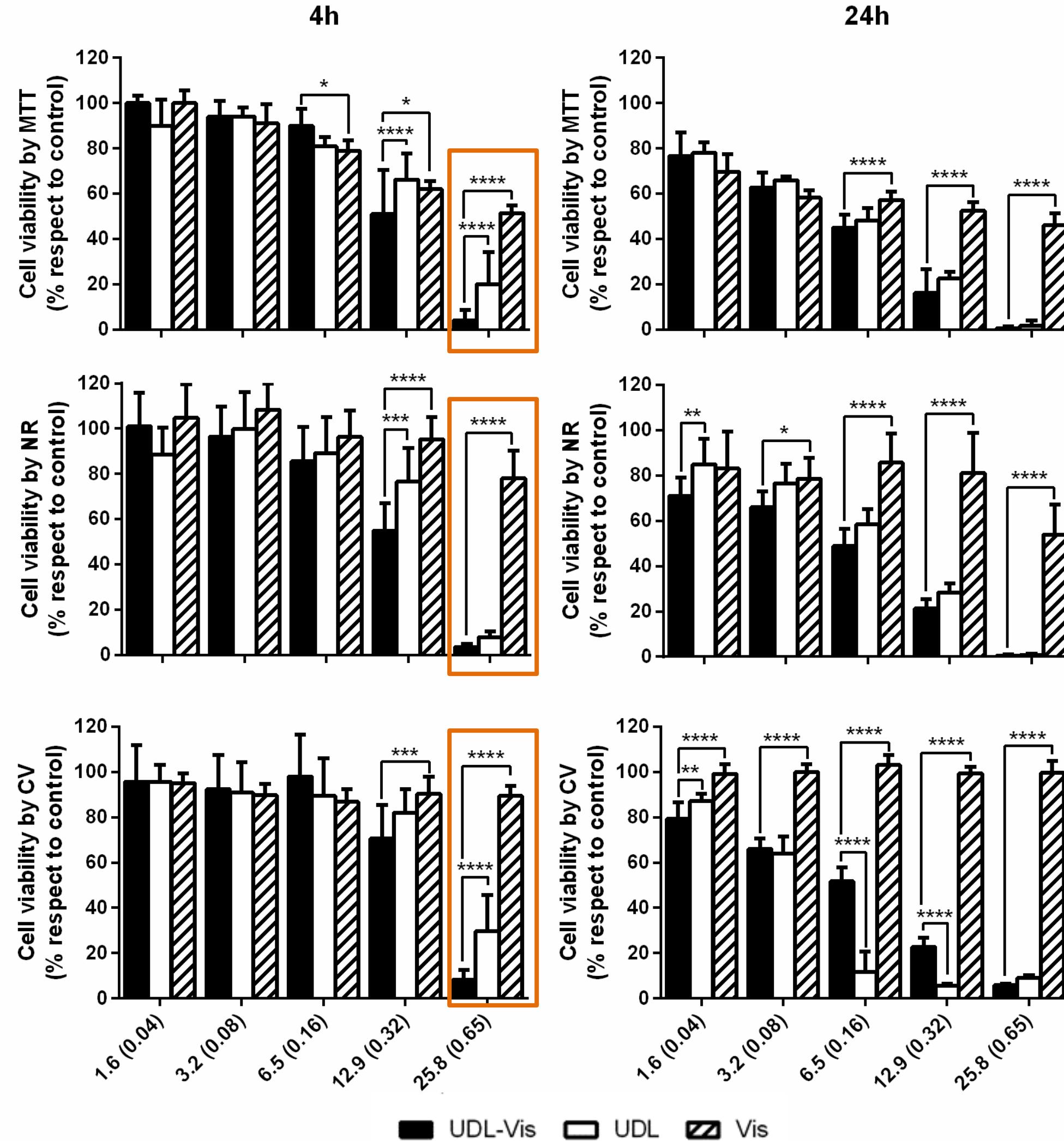
Confocal laser scanning
microscopy

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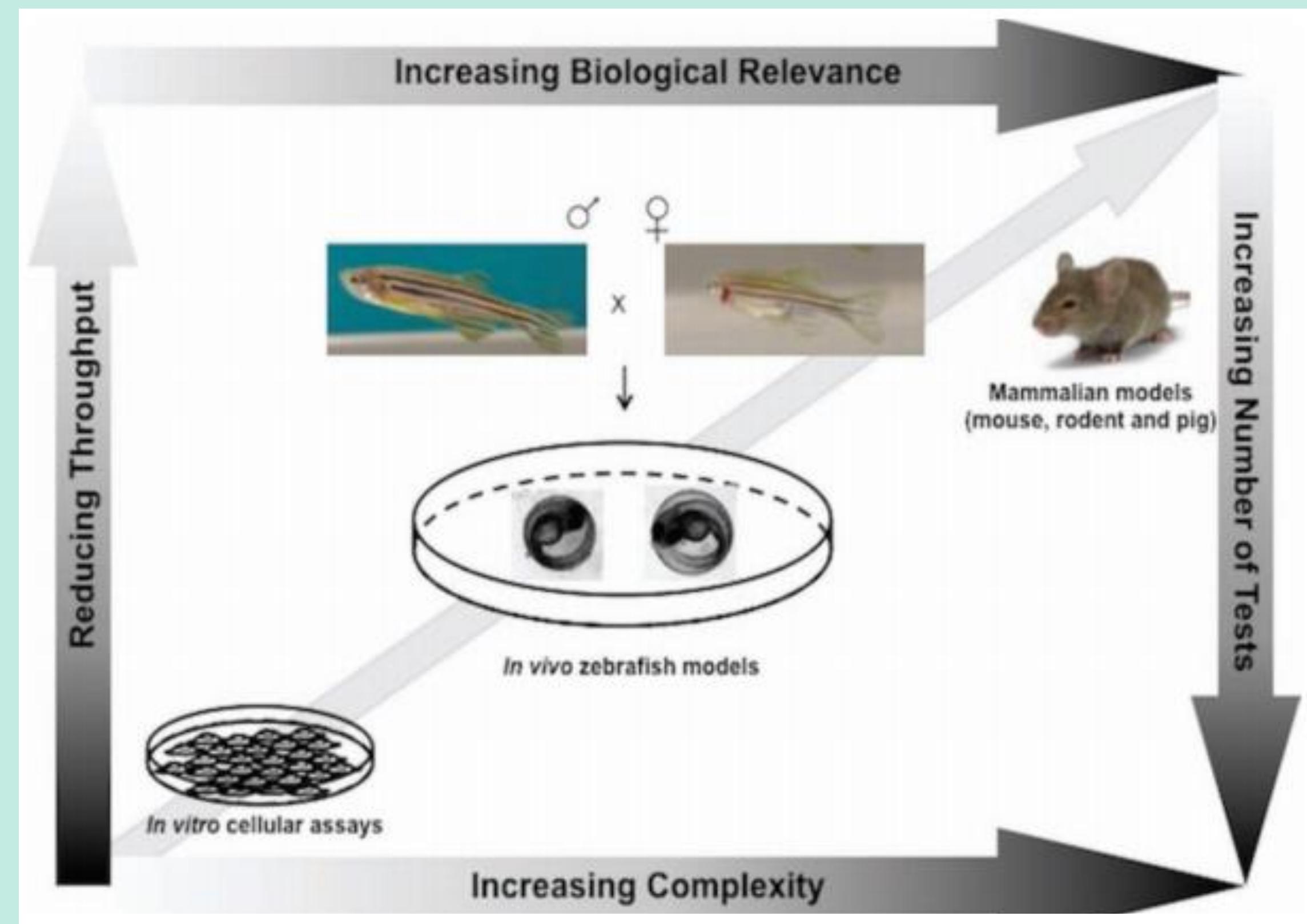
Cytotoxicity

The cytotoxicity of UDL-Vis compared with the free Vis was studied on HaCaT and SK-Mel-28 by MTT, neutral red and crystal violet. For both cell lines the nanoformulation was more cytotoxic.

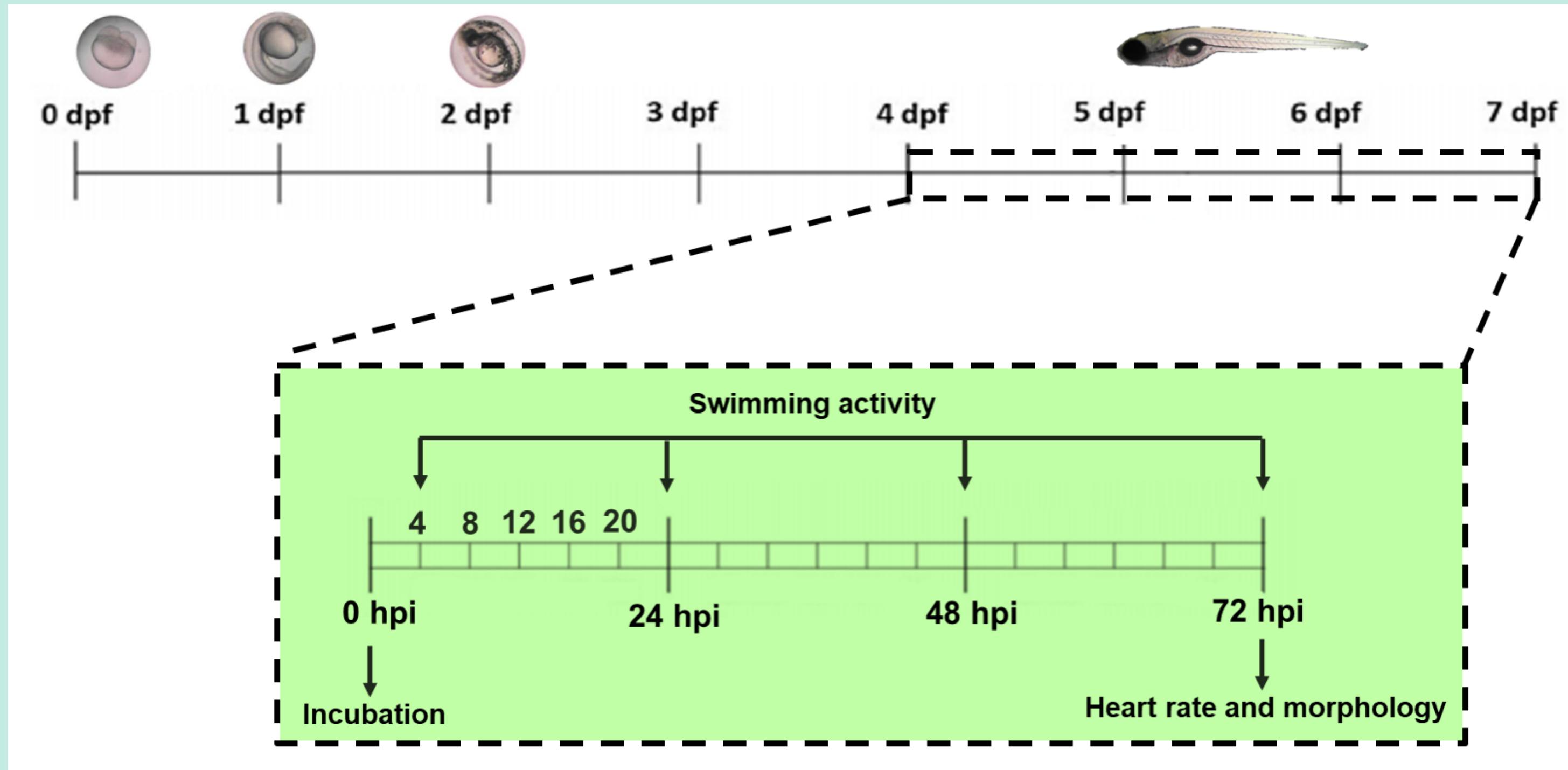
Percentage of cell viability of SK-Mel-28 after 4 and 24 h of incubation with UDL, UDL-Vis and free Vis determined by MTT, neutral red (NR) and crystal violet (CV). Concentrations are expressed as the concentration of SPC in mM and within the parenthesis the concentration of Vis in mg/ml. Data are presented as mean \pm SD ($n = 3$).



Zebrafish (*Danio rerio*)

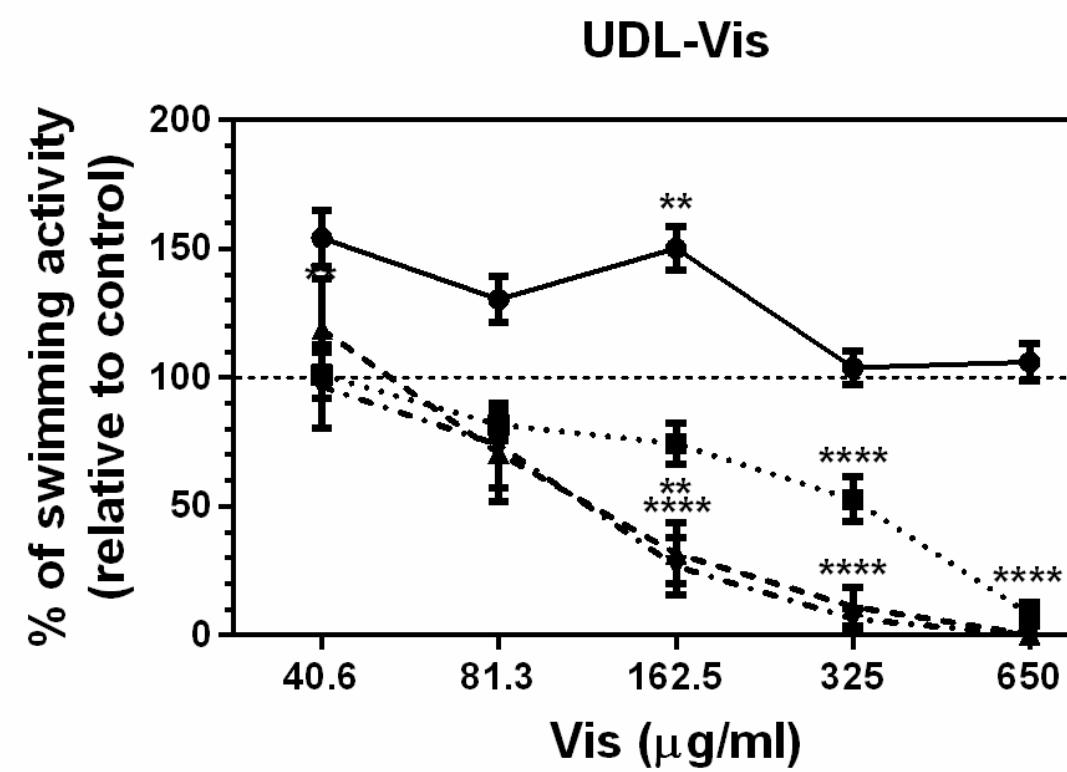
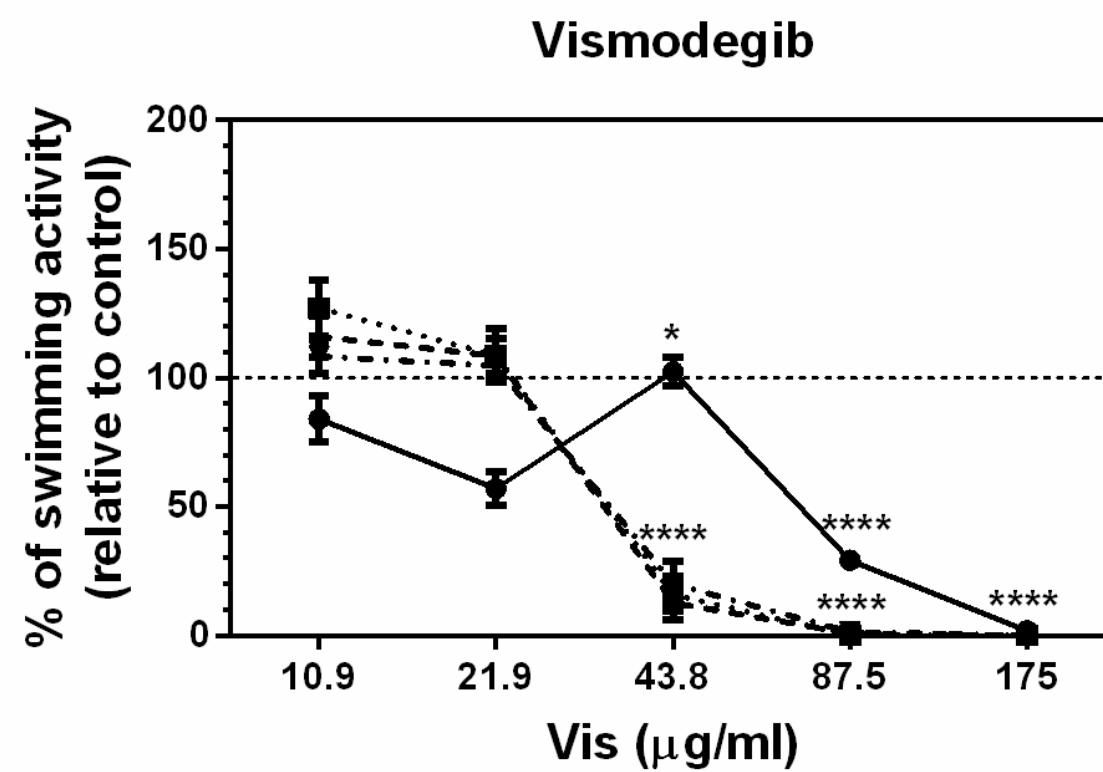


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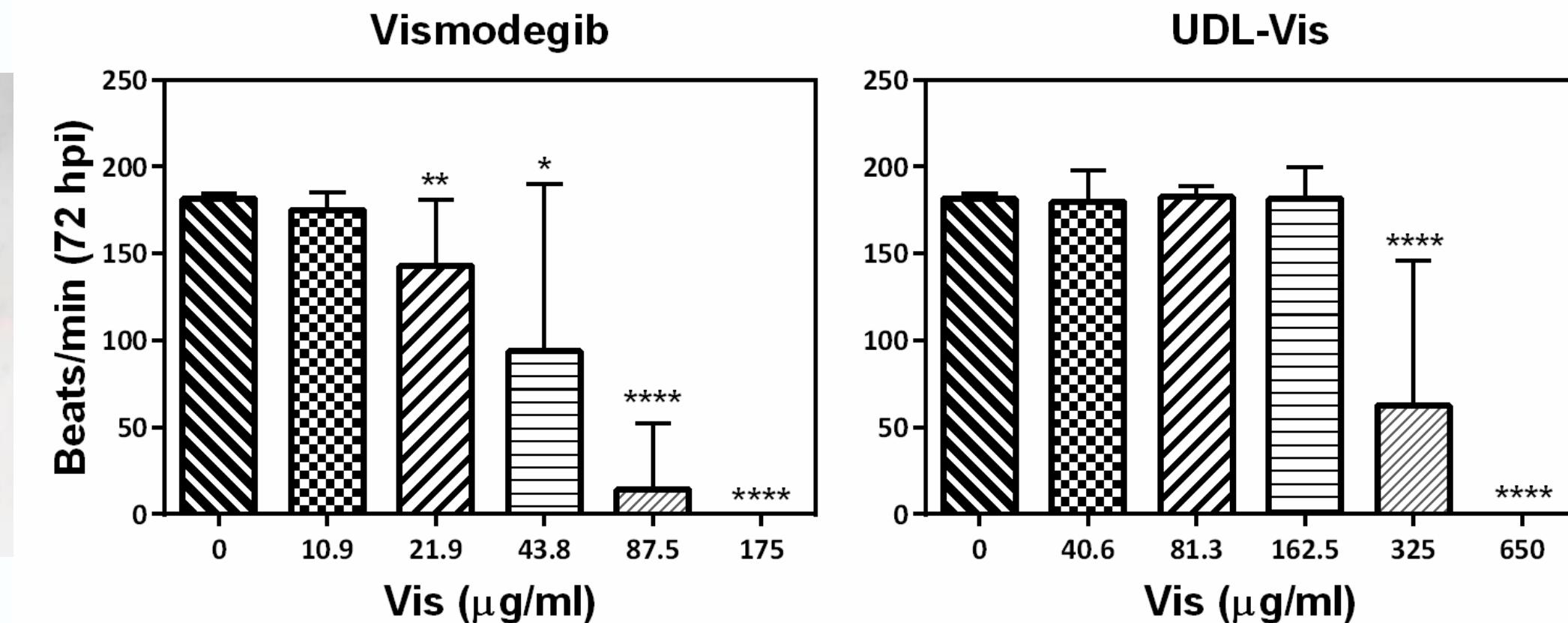
In vivo toxicological studies

Swimming activity



The nanoformulation was less toxic for larvae than the free drug

Alteration of the heart rate



Conclusions

- It was obtained a nanoformulation which can pass through the *stratum corneum*, delivering supra-therapeutical amounts of Vismodegib in the viable epidermis of the skin
- UDL-Vis showed to be effective for topical delivery of Vismodegib in views of the treatment of skin cancer lesions (even in early stages)
- This novel administration route could reduce the side effects reported after oral administration by the use of lower quantities of Vismodegib and site-specific delivery
- However, further studies assessing toxicity and antitumor activity *in vivo* should be performed

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Thank you

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