MOLECULAR CHARACTERIZATION OF CETACEAN SKIN – LAYING THE FOUNDATION TO DEVELOP CUTANEOUS BIOMARKERS

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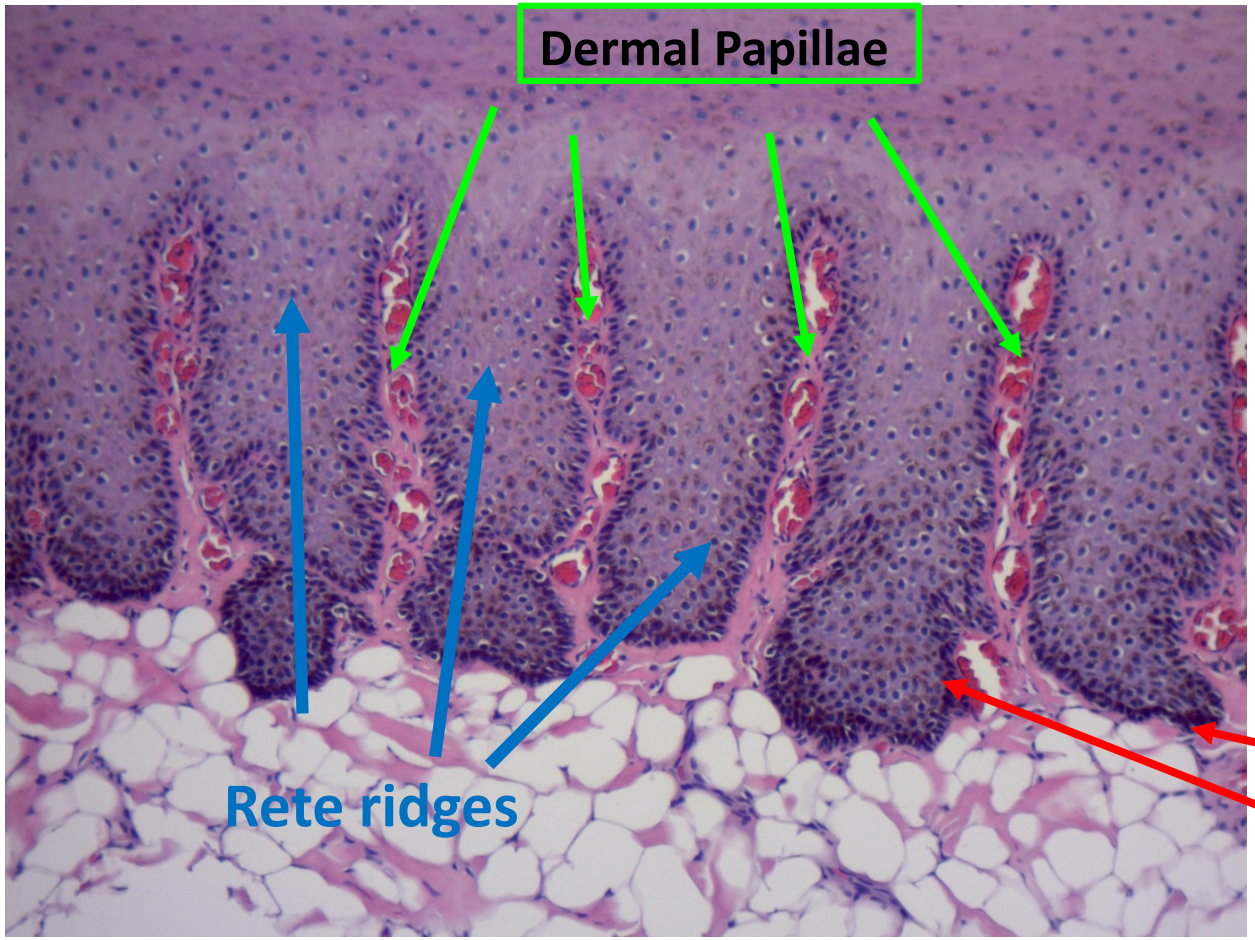
Mesoplodon species – poss Gervais' beaked whale

Cookie cutter shark wounds

Normal Cetacean skin

Epidermis
S. Externum
S. Spinosum
S. Germinativum
(basal layer)

Dermis



Basal epidermis layer

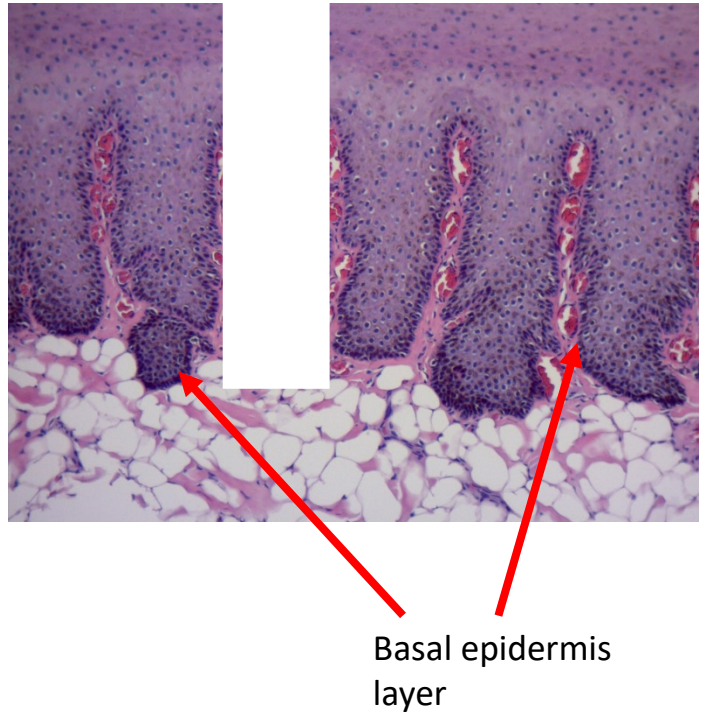
Human skin

Wound healing – *Tursiops*

(Bruce-Allen and Geraci, 1985; *Can. J. Fish Aquat Sci*)

- Basal germinal layer –
  - Within 24 hours undergoes increased mitoses, intercellular edema that breaks the intercellular connections, and pseudopodia bearing keratinocytes that move along over exposed dermis to cover skin lesion
- Stratum spinosum
  - 2-3 days, new (edematous) cells formed; span skin lesion; 4-20 cell layers thick
- Stratum externum –
  - Incompletely keratinized (retains nuclei; parakeratotic)
  - Completely closed by 3-4 days

At day 7, dermal papillae of relatively uniform size/shape restored.



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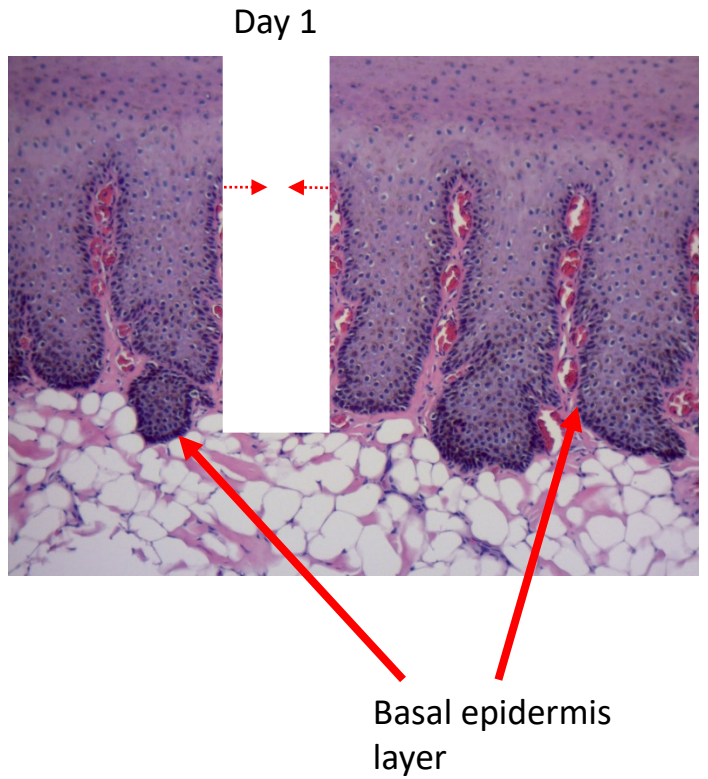

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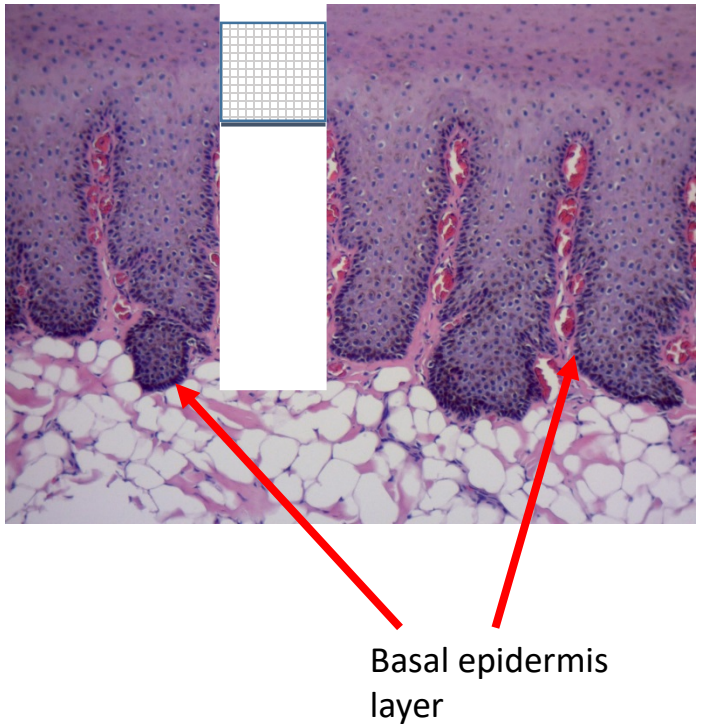
Day 2-3



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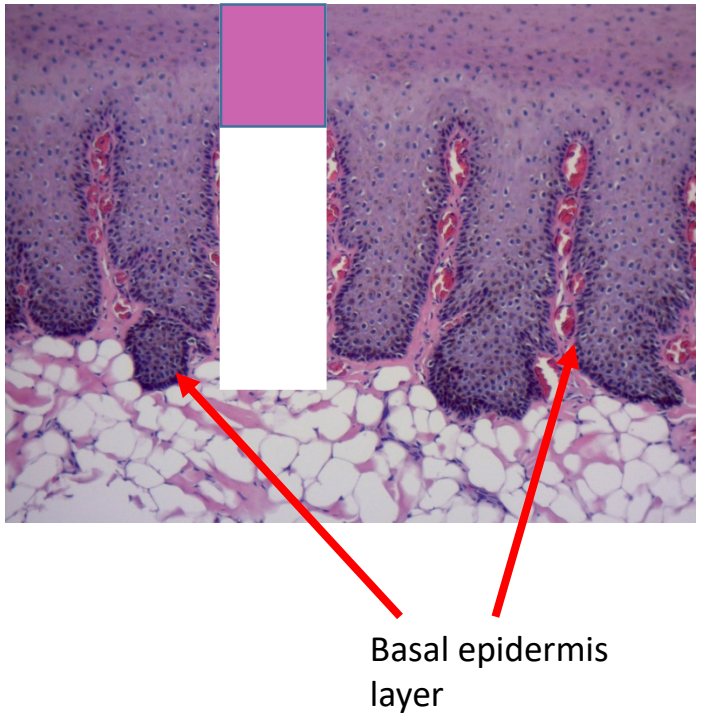
Day 3-4



Normal → Center of lesion

epidermis

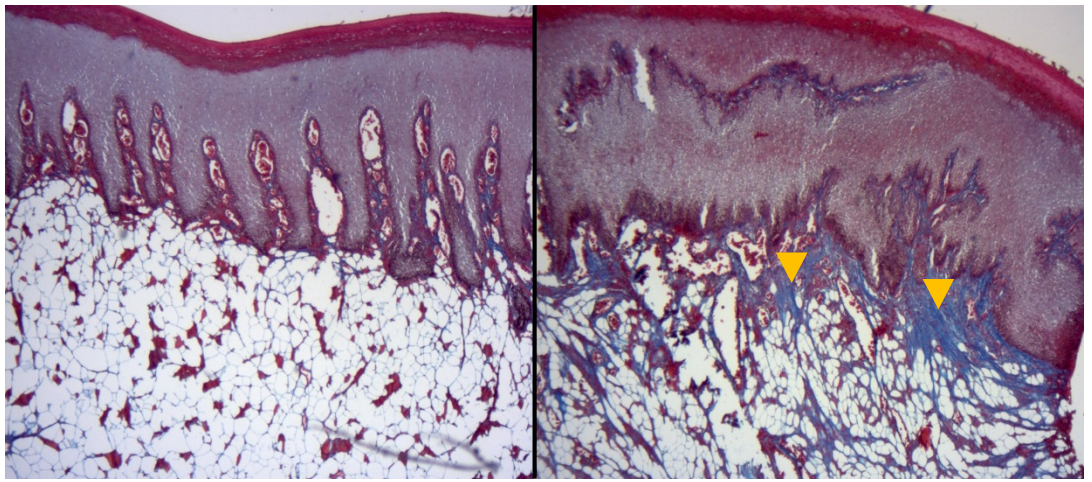
dermis

Center of lesion

Adipose cells (Fat) – white

Smooth muscle – yellow arrowhead

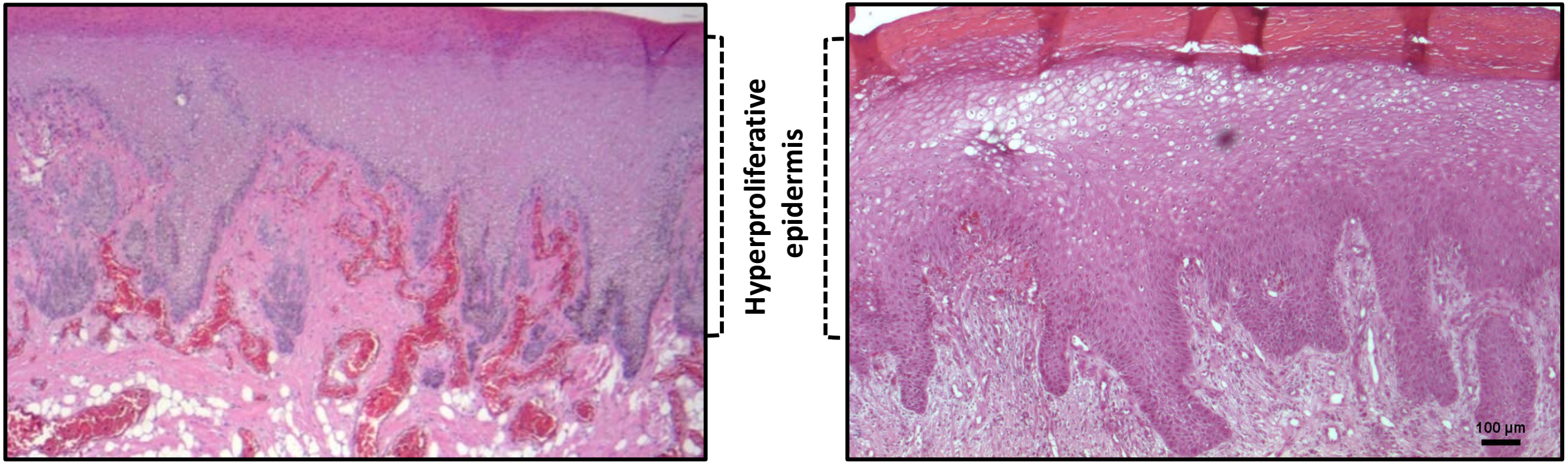
- pink in HE (above)
- blue in Trichrome stain (right)



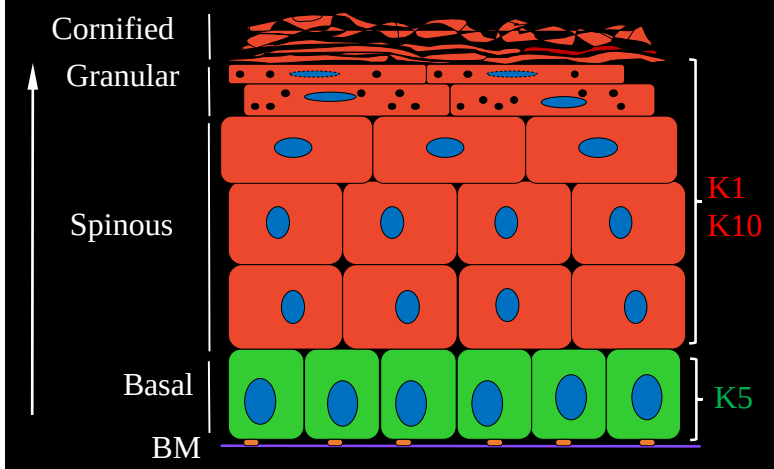
Comparison with human epidermis from non-healing chronic wound

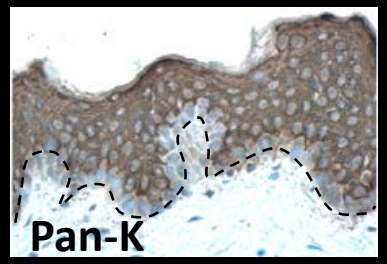
Cetacean lesion

Human non-healing wound



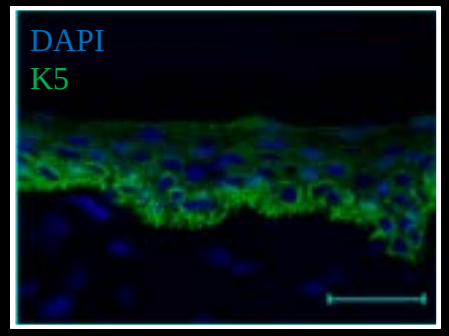
Homology of cetacean with human keratin 5



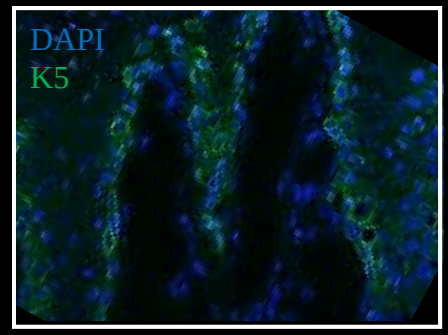


Human

Cetacean

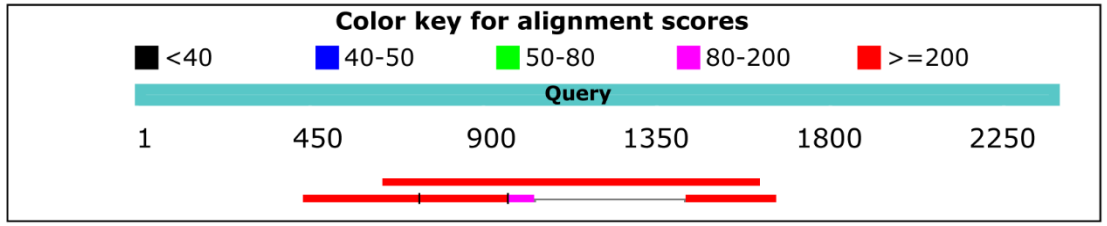


Human



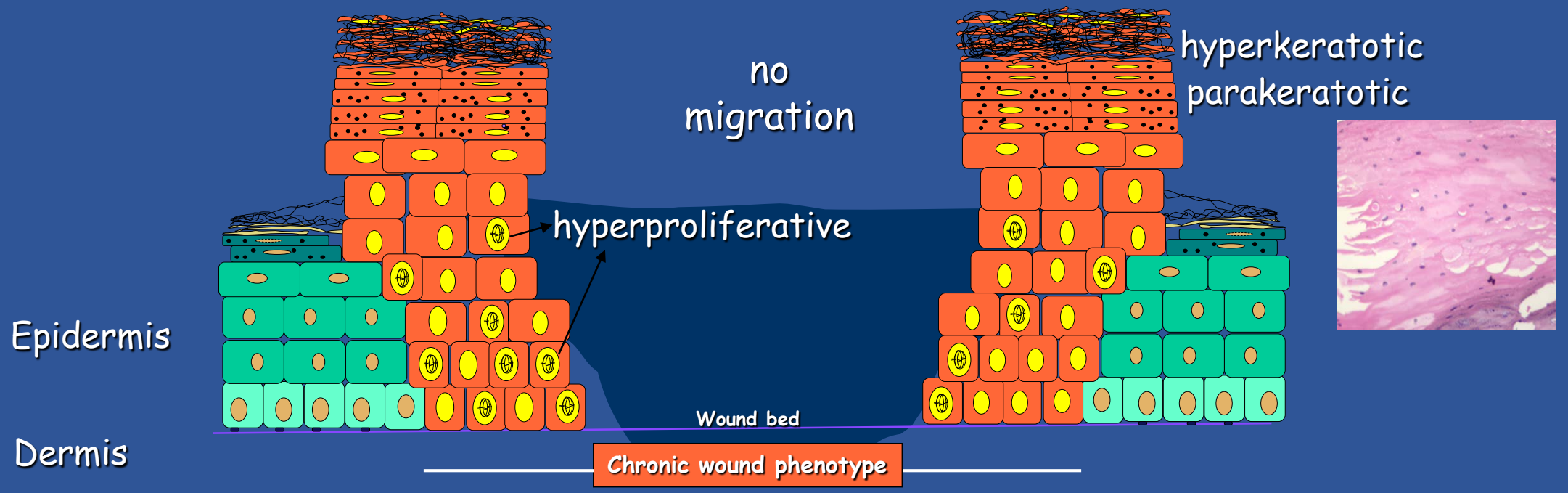
Cetacean

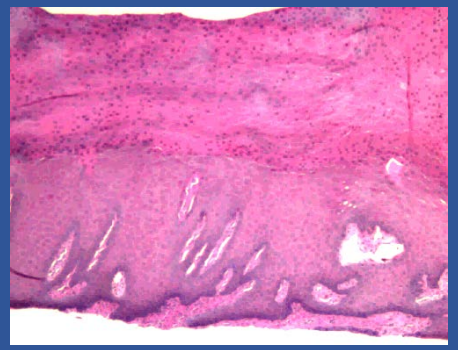
Distribution of the top 15 Blast Hits on 2 subject sequences



Description	Max score	Total score	Query cover	E value	Ident
Tursiops truncatus isolate MMES2002162SC unplaced genomic scaffold, NIST Tur_tru v1	501	501	41%	5e-139	77%

Histopathology of a human chronic wound:
Hyper-proliferation; loss of migration due to nuclear β-catenin

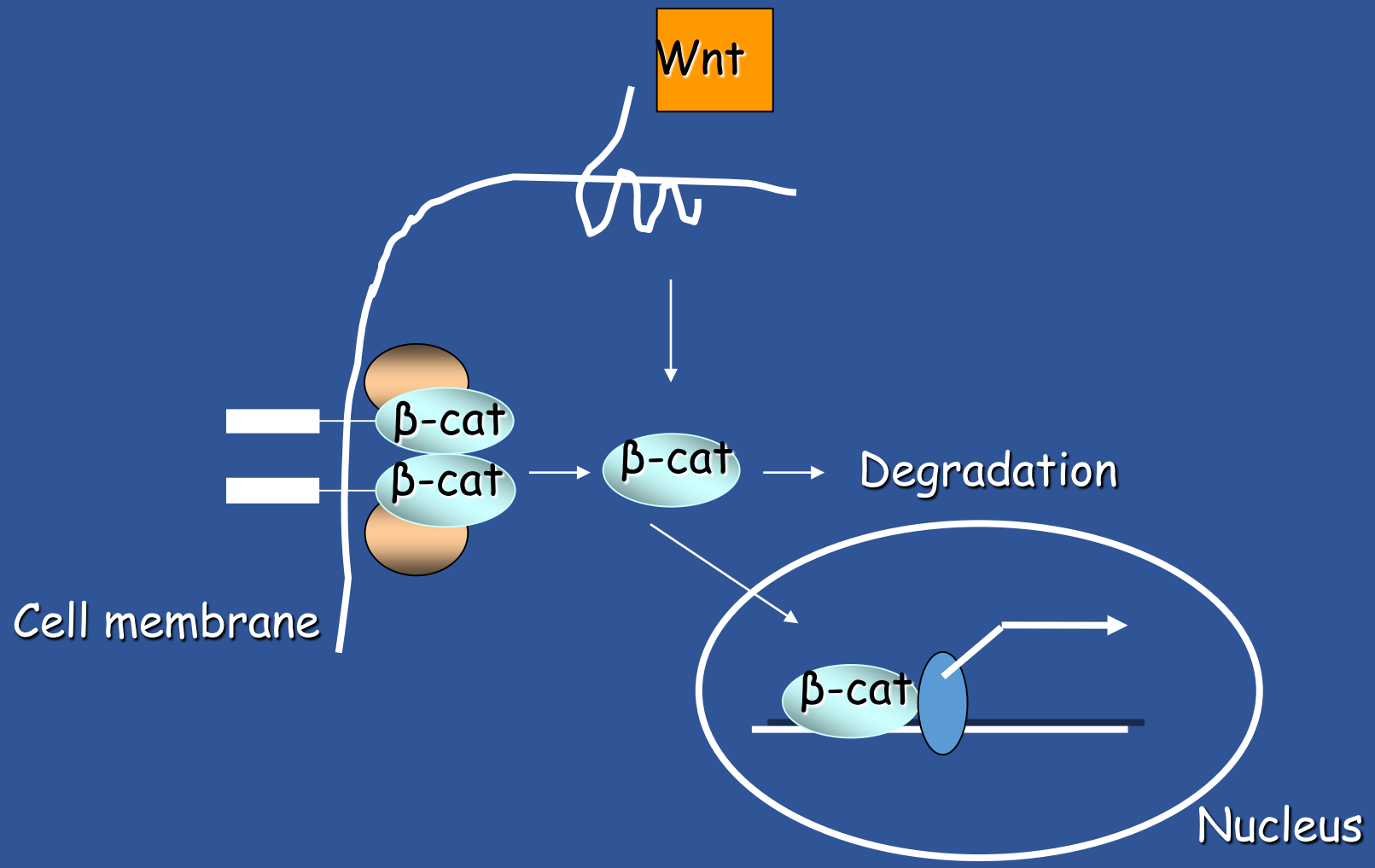




EPIDERMIS OF A HUMAN CHRONIC WOUND

Pastar I et al. Adv Wound Care. 2014.

Activation of the β – catenin Pathway

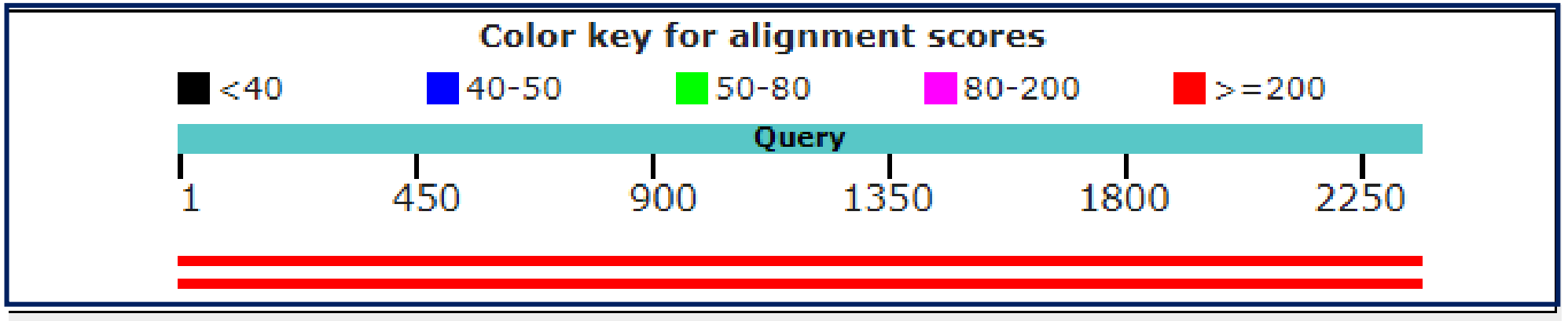


β-catenin as cutaneous biomarker

- The Wnt pathway
  - is important for skin homeostasis contributing to the maintenance/control of stem cells and cellular fate in the epidermal compartments
  - Controls ß-catenin activation

- Nuclear presence of β-catenin human tissue specimens is quantifiable by use of immunohistochemistry highlighting their feasibility as a tissue biomarker.

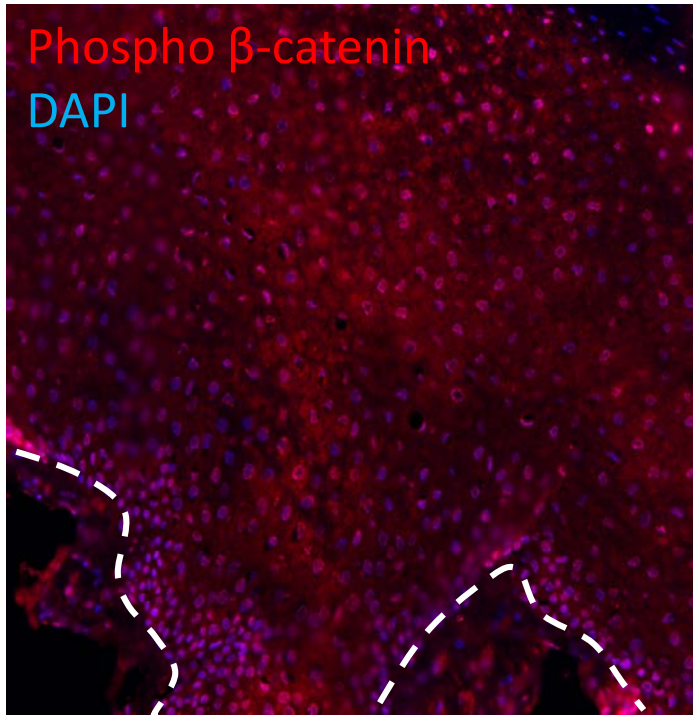
Comparative genomics identified cetacean gene homologous to human β-catenin



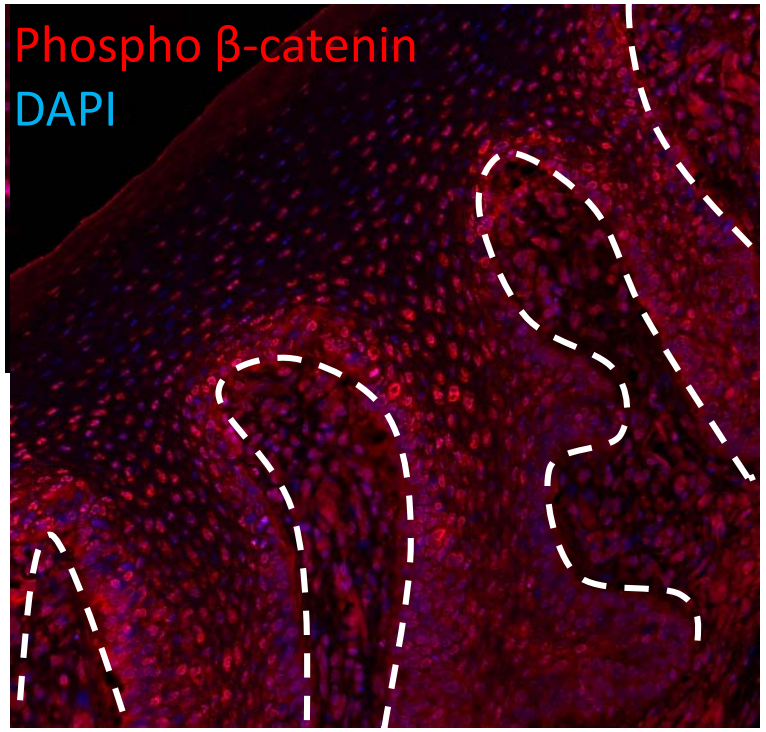
	Max score	Cover	Identity
Tursiops truncatus catenin beta 1 (CTNNB1), transcript	3823	100%	96%

Phosphorylated β-catenin is nuclear in the lesion of cetacean skin

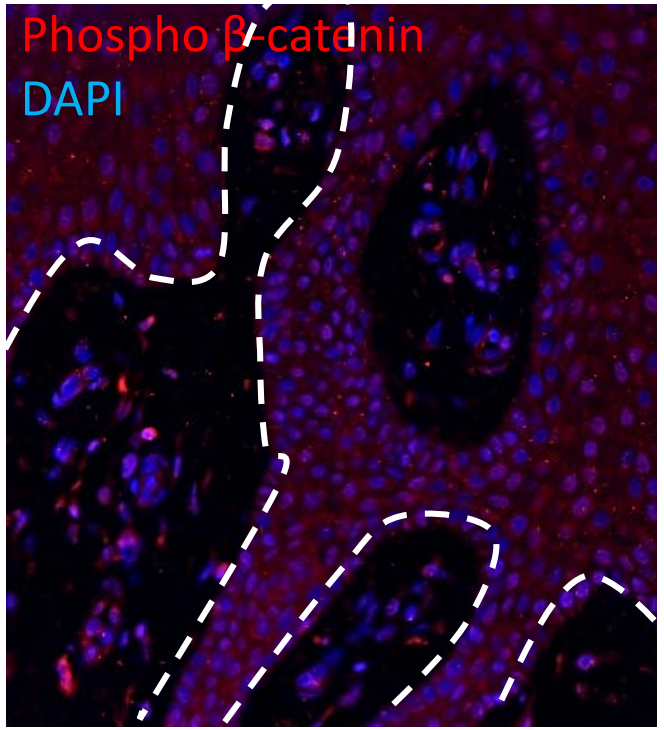
Cetacean lesional skin 1



Cetacean lesional skin 2



Human non-healing wound



Conclusions and future directions

- Strong nuclear β-catenin indicates activation of the skin cells and epidermal stem cells in cetacean skin
- Human keratin protein antibodies and β-catenin antibody nicely cross-react with cetacean skin
- Detailed molecular characterization of normal, acute, and chronic cetacean wounds possible
- Evaluation of skin for biomarker(s) to identify infectious or environmental stressors from dart biopsies

THANK YOU

Thanks to Lulu L Wang, Cheyanne Head, Irena Pastar

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