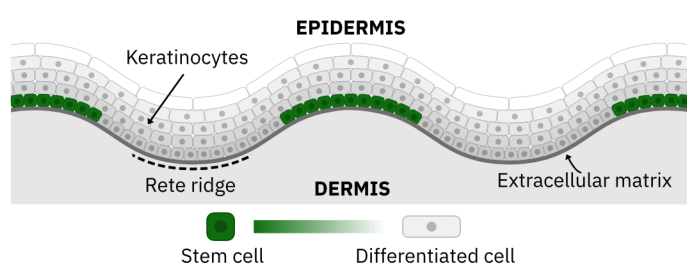


# How topography governs epidermal stem cell fate: role of curvature, migration and stretch

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## BACKGROUND



Human skin consists of the epidermis, which is composed of keratinocytes, and the dermis, which is the underlying connective tissue. Projections of the epidermis into the dermis, namely the rete ridges, serve as niches for undifferentiated keratinocytes called epidermal stem cells (Jones *et al.* 1995).

## NUCLEAR YAP AND LAMIN A/C LEVELS ARE HIGHER ON CONVEX CURVATURES

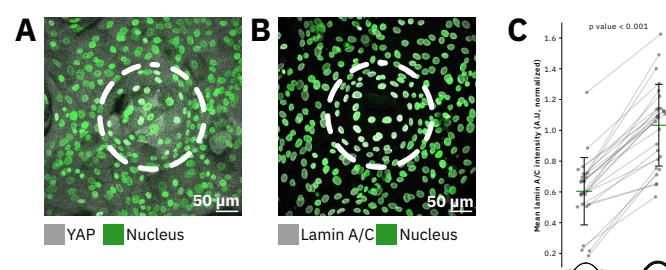


Figure 3: Keratinocytes grown on convex PDMS substrates stained for (A) YAP or (B) lamin A/C. The tip region is demarcated with a dashed circle. (C) Quantification of nuclear lamin A/C levels.

## H3K27me3 LEVELS ARE HIGHER ON CONVEX CURVATURES

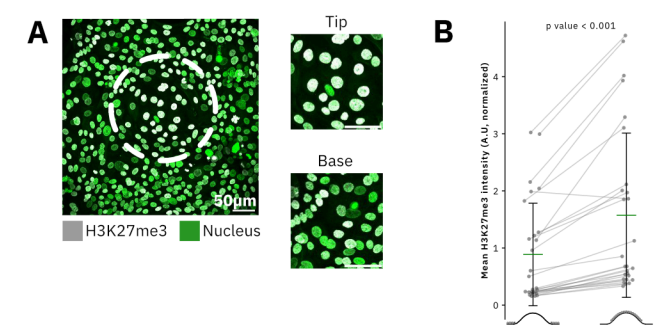


Figure 6: (A) Keratinocytes grown on convex PDMS substrates stained for H3K27me3. The tip region is demarcated with a dashed circle. (B) Quantification of nuclear H3K27me3 levels.

## APPROACH

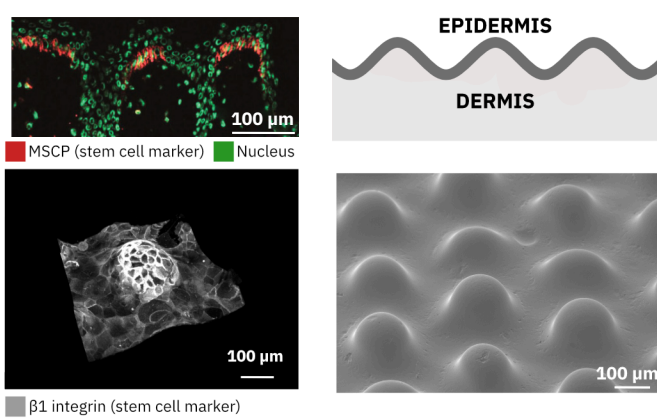


Figure 1: Polydimethylsiloxane (PDMS) substrates that mimic the undulations of the dermal-epidermal junction and stem cell patterning in human skin (Mobasseri *et al.*, 2019, Giangreco *et al.*, 2010).

## ADHERENS JUNCTIONS ARE UNDER TENSION ON CONVEX CURVATURES

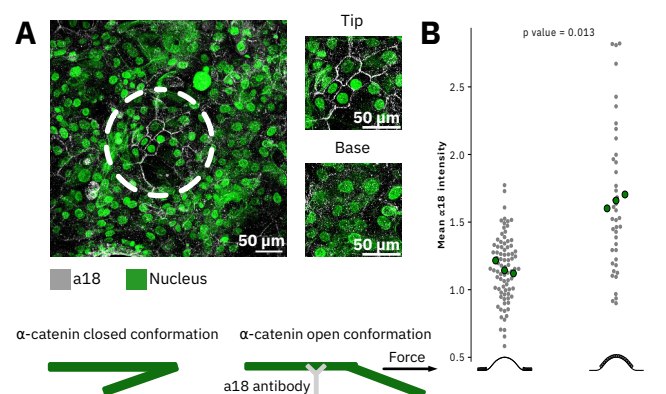


Figure 4: (A) Keratinocytes grown on convex PDMS substrates stained for the open conformation of  $\alpha$ -catenin using the a18 antibody. The tip region is demarcated with a dashed circle. (B) Quantification of a18 intensities at cell-cell borders.

## PATTERNING IS SENSITIVE TO THE DIRECTION OF CURVATURE

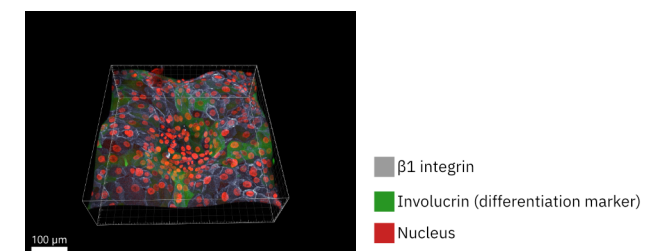
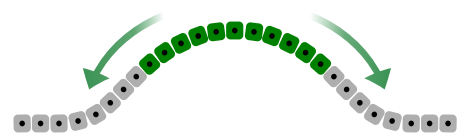


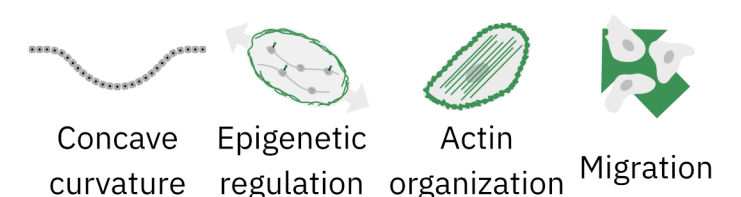
Figure 7: (A) Keratinocytes grown on concave PDMS substrates. Epidermal stem cells pattern on the edges of the curvature.

## HOW IS PATTERNING REGULATED?



Topographical curvature?  
Mechanical stretch?  
Preferential Migration?

## ONGOING AND FUTURE WORK



## FOCAL ADHESION MORPHOLOGY IS AFFECTED BY CONVEX CURVATURE

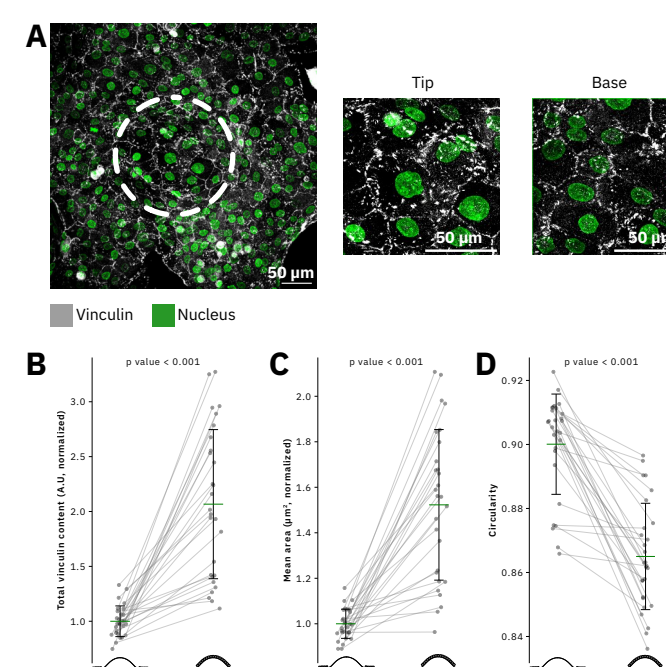


Figure 5: (A) Keratinocytes grown on convex PDMS substrates stained for vinculin. The tip region is demarcated with a dashed circle. Quantification of focal adhesion (B) vinculin content, (C) area and (D) circularity.

## NUCLEI ARE ELONGATED ON CONVEX CURVATURES

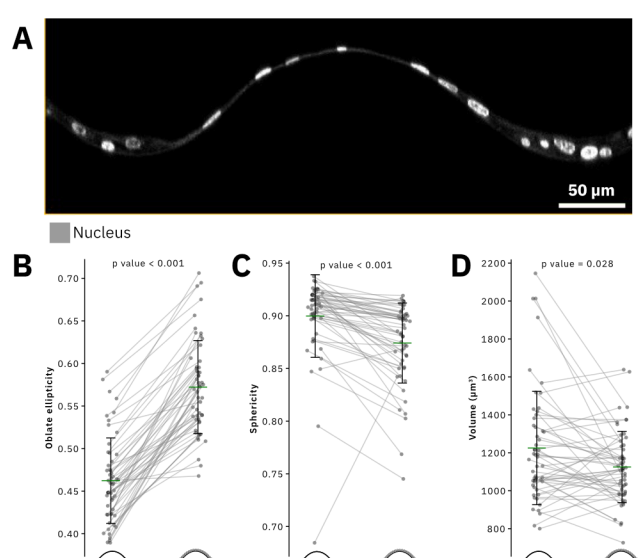


Figure 2: (A) Orthogonal slice of a convex feature. Quantification of nuclear (B) ellipticity, (C) sphericity and (D) volume.

## ACKNOWLEDGEMENTS

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## REFERENCES

- P. H. Jones, S. Harper, F. M. Watt, *Cell*. 80, 83–93 (1995).
- S. A. Mobasseri *et al.*, *Acta Biomater.* 87, 256–264 (2019).
- A. Giangreco, S. J. Goldie, V. Failla, G. Saintigny, F. M. Watt, *J. Invest. Dermatol.* 130, 604–608 (2010).

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