



Crosstalk between HIF-1 α and SIRT-1 is bolstered by the natural ingredient bakuchiol but not retinol

Hemali Gunt, PhD¹, Manpreet Randhawa, PhD², Krzysztof Bojanowski, PhD³, and
Ratan K. Chaudhuri, PhD²

¹Burt's Bees, Durham, NC; ²Sytheon, Boonton, NJ; ³Sunny Biodiscovery, Santa Paula, CA

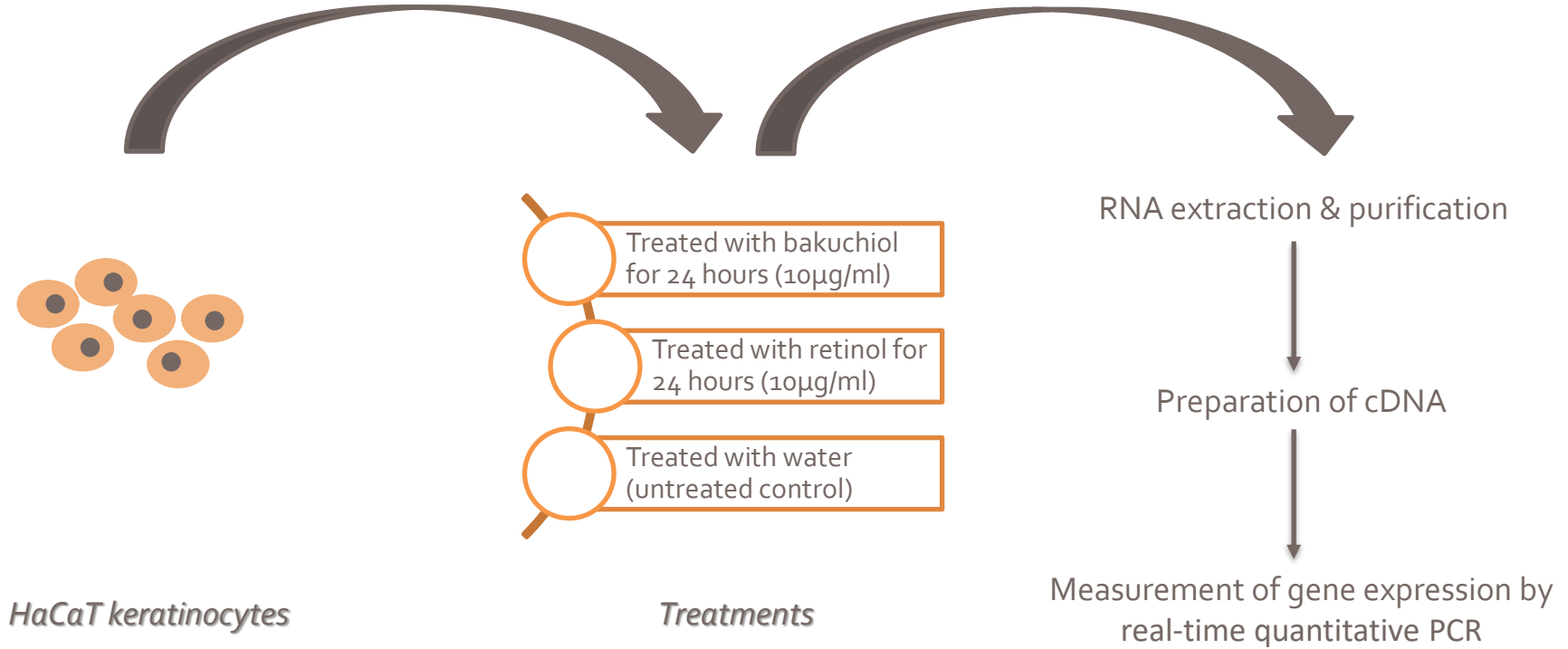
Background

- Sirtuins comprise one of the promising targets for preventing diseases and reversing some aspects of aging. Sirtuins are NAD-dependent deacylases and known to regulate diverse cellular and pathological processes including cellular senescence, DNA repair, inflammation, and aging. SIRT-1 modulates cellular responses to hypoxia by deacetylating HIF-1 α , which regulates HIF activity in response to hypoxic stress. HIF acts as a transcriptional regulator of genes involved in survival during periods of low oxygen (the hypoxic response). ¹
- Both Sirtuin and HIF-1 α levels decrease as a function of age. With age, HIF-1 α induces a deficit in mitochondrial biogenesis, which impairs energy-dependent cellular processes, including cell and tissue repair. Levels of SIRT-1 decrease in both transcriptional and posttranscriptional stages during aging, which attenuates mitochondrial biogenesis and causes age-related diseases. ²
- Over the past two decades, various biochemical and genetic studies have helped expand our knowledge of hypoxia at the cellular and molecular levels. Hypoxia contributes to functional decline during the aging process. HIF pathways crosstalk with sirtuins in hypoxia and aging.

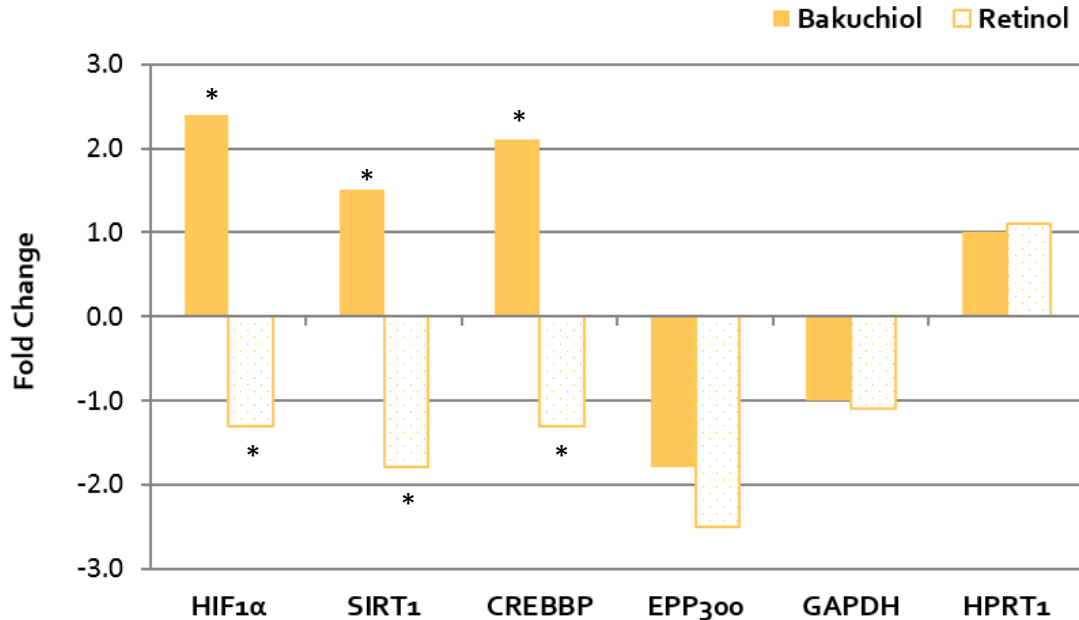
Objective

- To investigate the upstream mechanisms by which Bakuchiol (Sytenol A), a recently discovered natural alternative to Retinol, functions to reverse clinical signs of skin aging, by evaluating its effects on mitochondrial aging-related gene expression in human keratinocytes.

Methods



Results



* $p \leq 0.05$

Gene expression normalized to GAPDH and HPRT1
(housekeeping genes)

- *Bakuchiol significantly increased both HIF-1α (+2.4 fold change) and SIRT-1 (+1.5 fold change) gene expression*
- *Retinol showed an opposite trend decreasing HIF-1α (-1.3 fold change) and SIRT-1 (-1.8 fold change)*
- *CREBBP, a tumor suppressor gene, was also upregulated significantly by bakuchiol (+2.1 fold change) but not by retinol (-1.3 fold change)*

Conclusions

- The findings indicate the ability of bakuchiol, but not retinol, to upregulate expression of SIRT-1 and HIF-1 α in human keratinocytes.
- The results imply that bakuchiol may partly exert anti-aging benefits through pathways not supported by retinol, a long-held standard in helping reverse clinical signs of aging.

References

1. Yeo, EJ. Hypoxia and aging. *Exp Mol Med* 51, 1–15 (2019).
2. Pagani A, Aitzetmüller MM, Brett EA, König V, Wenny R, Thor D, Radtke C, Huemer GM, Machens HG, Duscher D. Skin Rejuvenation through HIF-1 α Modulation. *Plast Reconstr Surg*. 2018 Apr;141(4):600e-607e.