



S-BIOMEDIC

THE POWER OF YOUR SKIN MICROBIOME

Bernhard Paetzold , CSO



S-BIOMEDIC

At S-Biomedic, we develop novel dermatology solutions derived from the skin microbiome.

We tap into our patented technology platform to enhance the own power of your skin.

Our pioneer product contains live skin probiotics to restore the microbiome health in acne sufferers.



JLABS@BE in Belgium

Beiersdorf

Collaboration and License Agreement



Funding to-date over €5.4 mln

OVERVIEW



- Short history of the microbiome and their impact on ageing
- Introduction to Cutibacterium Acnes and its abundance during ageing
- Molecular interaction points between *C. acnes* and the host in the context of ageing
 - Autophagy
 - Sebum production
 - ROS induced DNA damage
- Closing and Acknowledgements

THE ORIGIN

Once upon a time...



4th Century China

"Yellow soup" to treat food poisoning & diarrhea



Portraiture of Ge Hong (葛洪)

Sharing under the pulic domain:
[Hannah~commons wiki / et.wikipedia.org](https://commons.wikimedia.org/wiki/File:Ge_Hong.jpg)

GUT MICROBIOME TRANSPLANTATION

History, concept and success in 2013



4th Century China

"Yellow soup" to treat food poisoning & diarrhea

2004

Next Generation Sequencing: 454/Illumina

2007

Establishment of Human Microbiome Project

2013 →

Successful FMTs for *Clostridium difficile* infection

2013

FDA allows FMT to treat *C. difficile* infection

2014 →

FMT trials for IBD, metabolic syndrome & neurological conditions

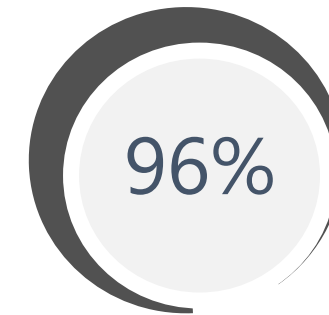


Healthy donor

Faecal transplant



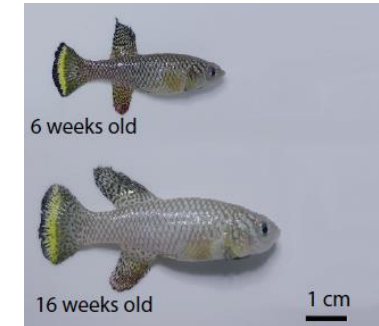
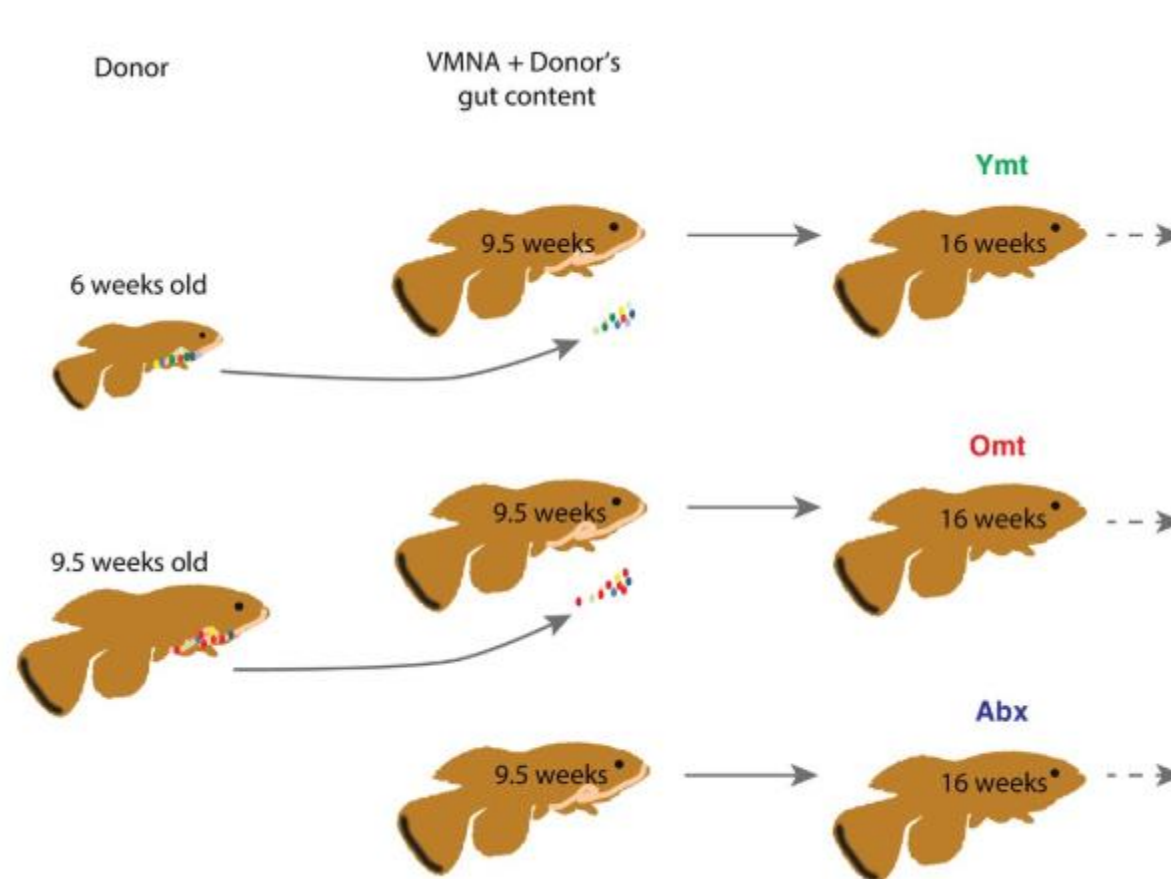
CDI patient



FMT success in CDI

CAN THE MICROBIOME HAVE AN IMPACT ON HOW WE AGE?

Regulation of Life Span by the Gut Microbiota in Killifish



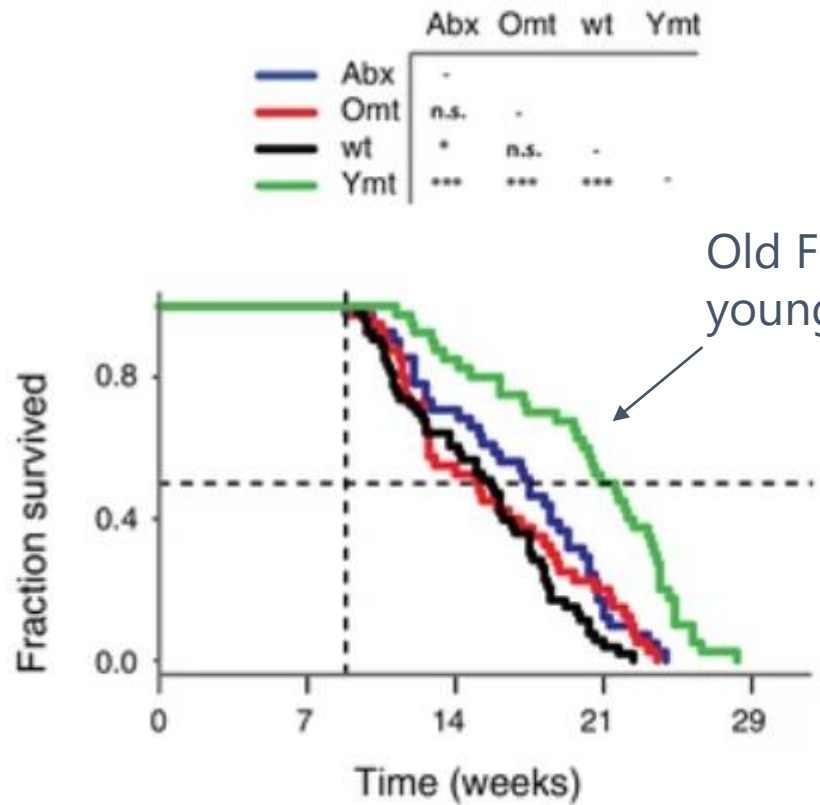
Smith, Patrick, David Willemsen, Miriam Popkes, Franziska Metge, Edson Gandiwa, Martin Reichard, and Dario Riccardo Valenzano. 2017. "Regulation of Life Span by the Gut Microbiota in the Short-Lived African Turquoise Killifish." Edited by Andrew Dillin. *ELife* 6 (August): e27014. <https://doi.org/10.7554/eLife.27014>.

CAN THE MICROBIOME HAVE AN IMPACT ON HOW WE AGE?

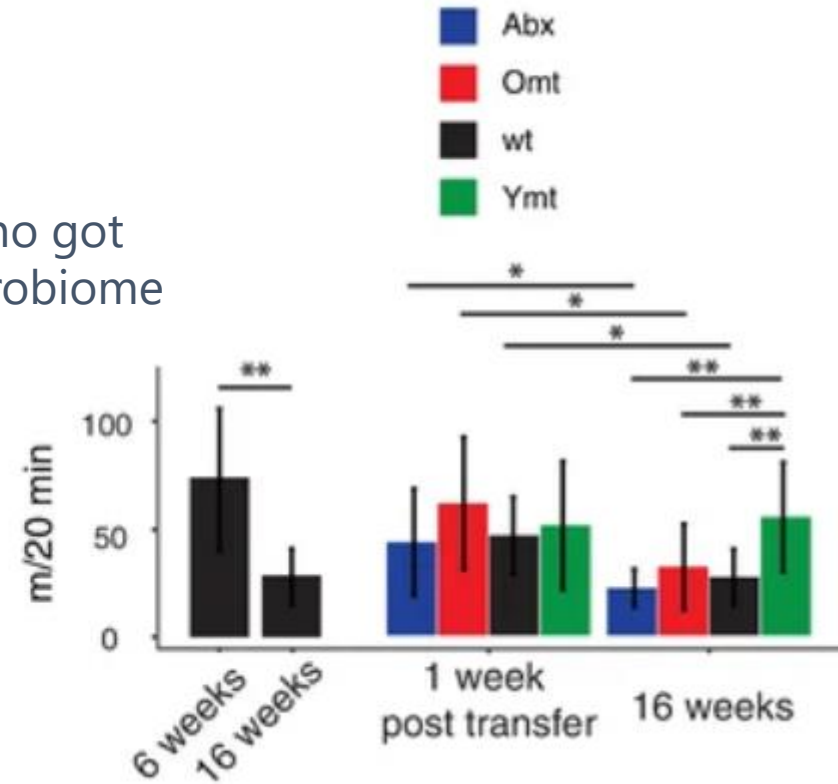
Regulation of Life Span by the Gut Microbiota in Killifish



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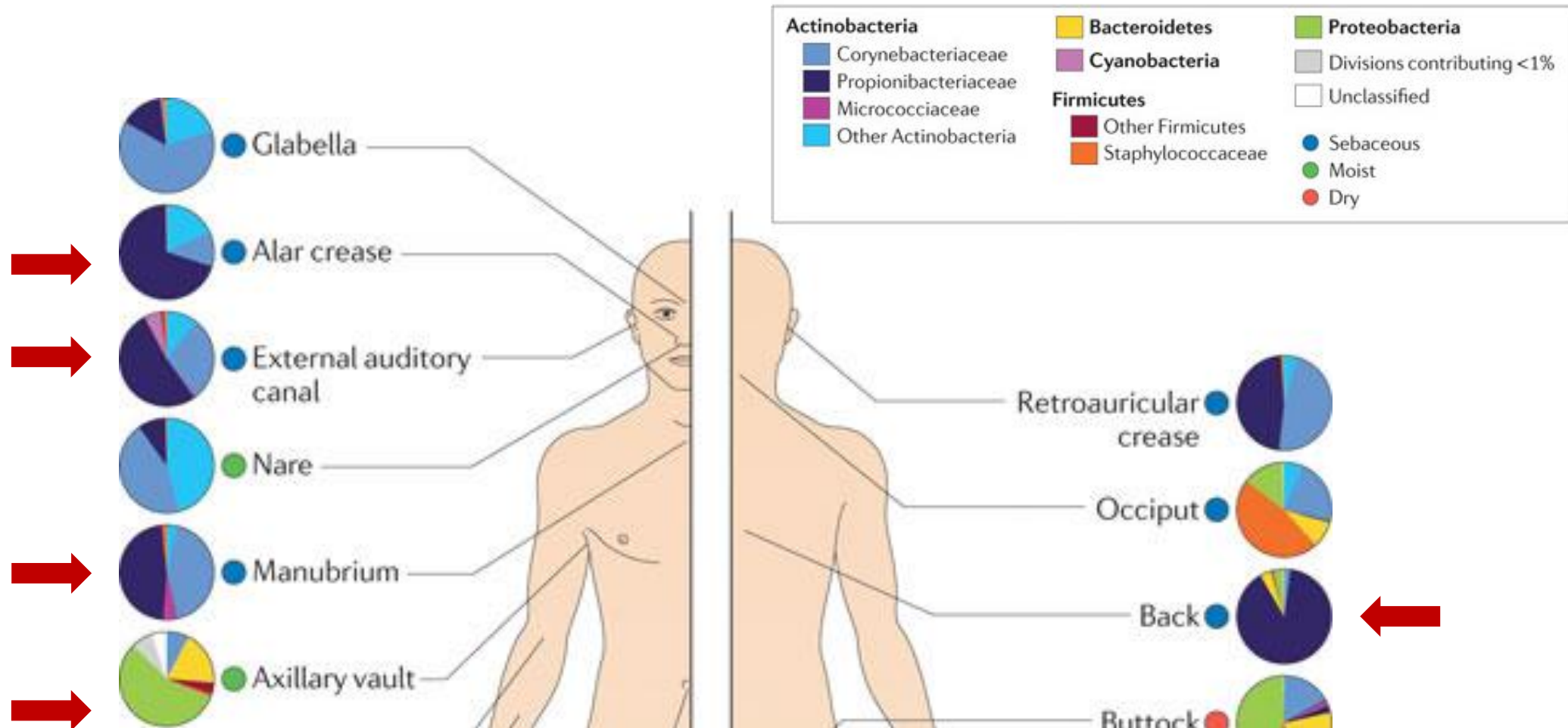
C



Smith, Patrick, David Willemsen, Miriam Popkes, Franziska Metge, Edson Gandiwa, Martin Reichard, and Dario Riccardo Valenzano. 2017. "Regulation of Life Span by the Gut Microbiota in the Short-Lived African Turquoise Killifish." Edited by Andrew Dillin. *ELife* 6 (August): e27014. <https://doi.org/10.7554/eLife.27014>.

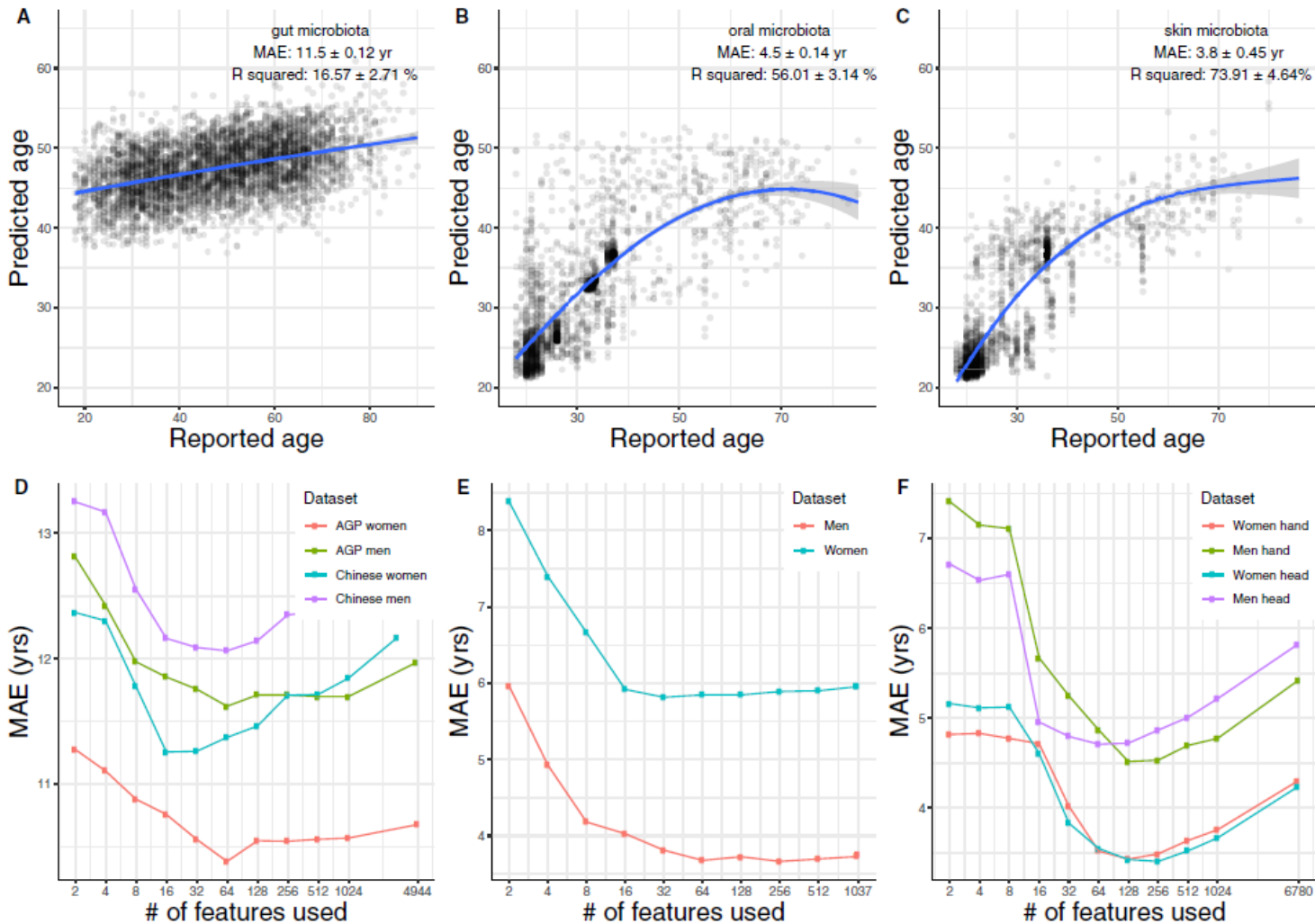
FACIAL MICROBIOME

the skin microbiome is different than the gut



SKIN MICROBIOME AND AGE, ARE THEY CONNECTED?

the skin microbiome is the best to predict the chronological age



“Interestingly, taxa enriched in young individuals (18 to 30 years) tend to be more abundant and more prevalent than taxa enriched in elderly individuals (60 yrs), suggesting a model in which physiological aging occurs concomitantly with the loss of key taxa over a lifetime, enabling potential microbiome-targeted therapeutic strategies to prevent aging.”

Huang, Shi, Niina Haiminen, Anna-Paola Carrieri, Rebecca Hu, Lingjing Jiang, Laxmi Parida, Baylee Russell, et al. 2020. “Human Skin, Oral, and Gut Microbiomes Predict Chronological Age.” *MSystems* 5 (1). <https://doi.org/10.1128/mSystems.00630-19>.

SHOW ME YOUR SKIN MICROBIOME I TELL YOU YOUR AGE

the skin microbiome is the best to predict the chronological age



Huang, Shi, Niina Haiminen, Anna-Paola Carrieri, Rebecca Hu, Lingjing Jiang, Laxmi Parida, Baylee Russell, et al. 2020. "Human Skin, Oral, and Gut Microbiomes Predict Chronological Age." *MSystems* 5 (1). <https://doi.org/10.1128/mSystems.00630-19>.

SUMMARY



The microbiome has been used since centuries as tool to treat disease

With the advent of NGS the research in this direction exploded

In Killifish the gut microbiome can have a profound influence on lifespan

The skin microbiome composition is strongly connected to how we age

CUTIBACTERIUM ACNES
THE KEY TO THE FACIAL MICROBIOME

Formerly known as *Propionibacterium acnes*

Scholz, C.F.P., and Kilian, M. (2016).

International Journal of Systematic and Evolutionary Microbiology.



CUTIBACTERIUM

the good



lives deep in the skin within the reach of live skin cells which makes it a powerful delivery tool



secretes strong antioxidant which protects the skin from harmful influence like radicals and UV radiation

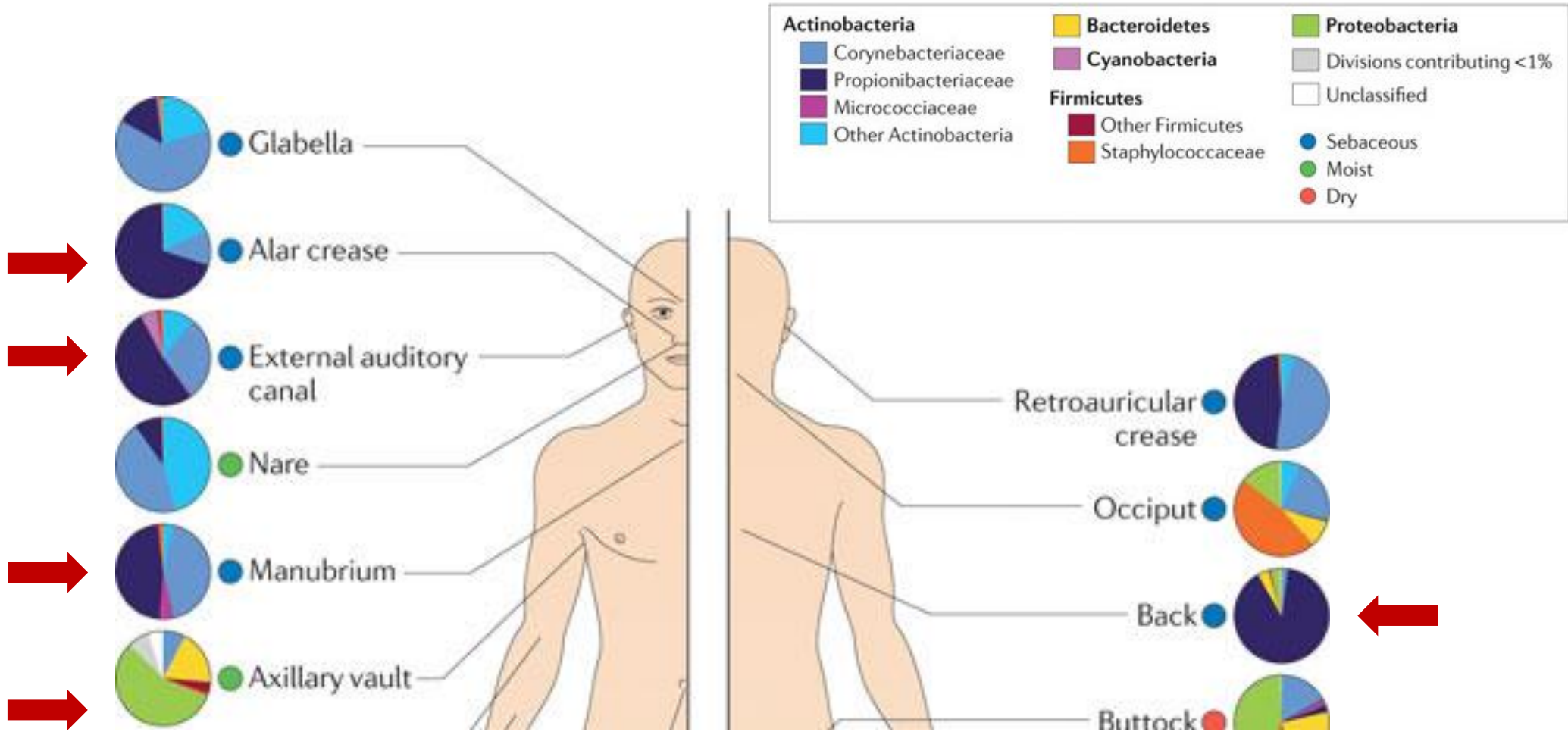


various strains influence sebum composition and sebum production



influences skin hydration

CUTIBACTERIUM THE MOST ABUNDANT SPECIES OF THE FACIAL MICROBIOME



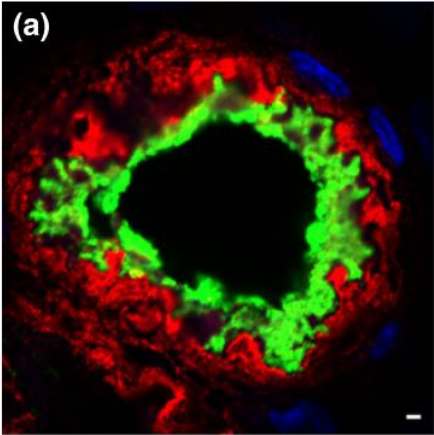
Elizabeth A. Grice & Julia A. Segre
 Nature Reviews Microbiology 9, 244-253 (April 2011)

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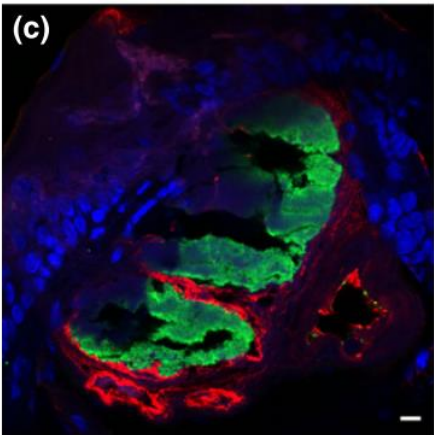
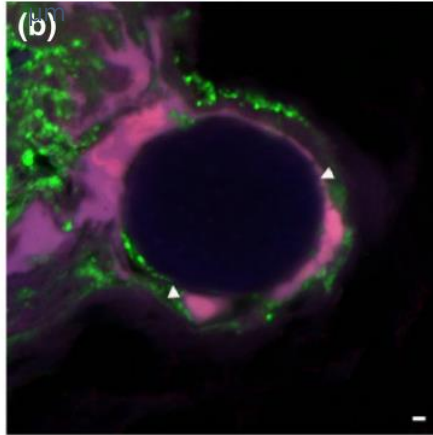
CUTIBACTERIUM HABITAT

Because of its natural habitat in the follicle *C. acnes* is constantly interacting with the highly active molecules contained in natural sebum. It is both influenced by sebum but also changes sebum through its metabolism

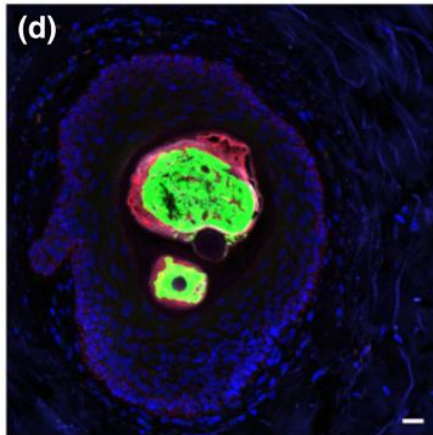
Attachment of *C. acnes* to the follicle wall; scale bar 2 μ m



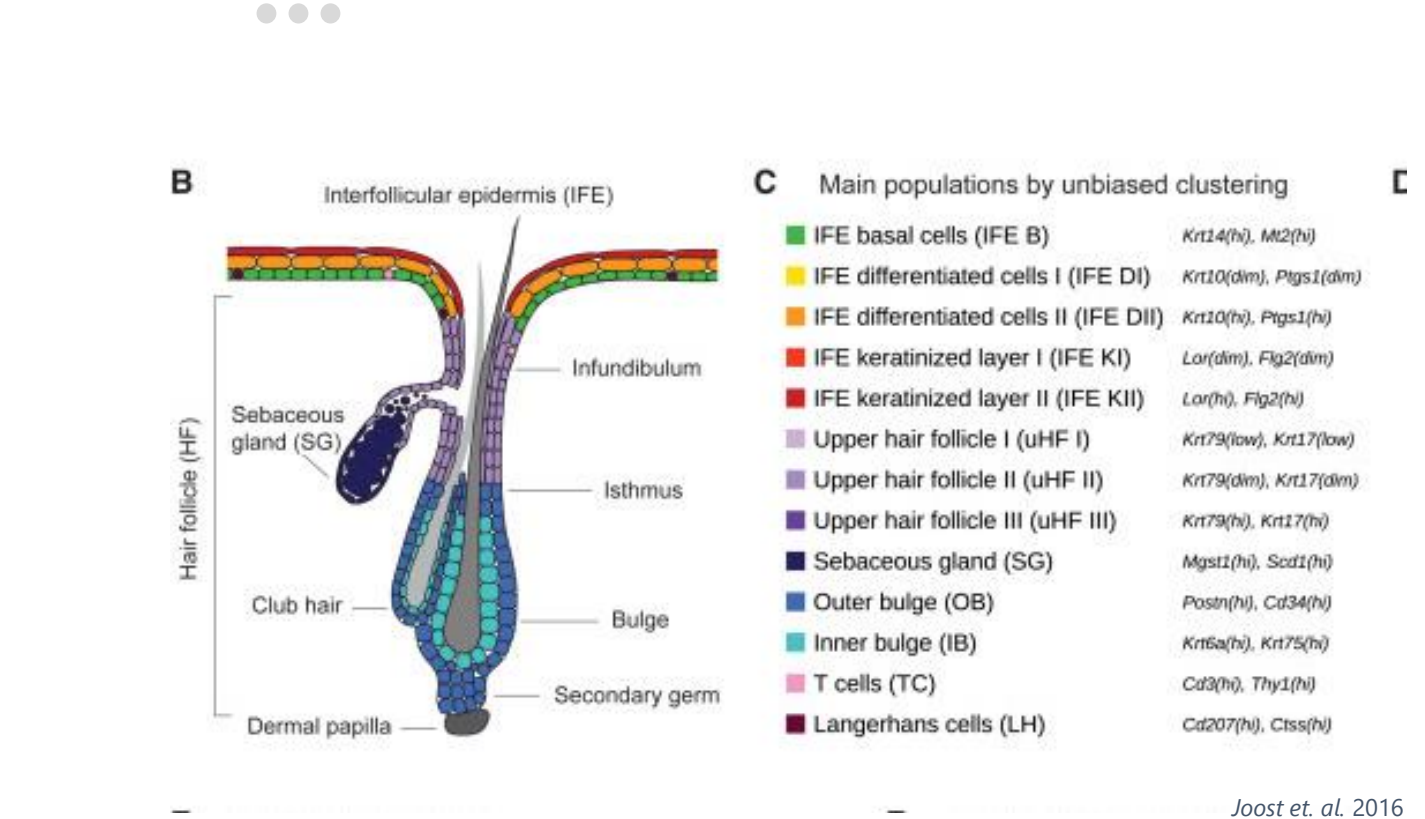
Attachment of *C. acnes* to the hair shaft, arrow heads point towards the hair shaft; scale bar 2 μ m



C. acnes biofilm spreading over nearly the entire lumen of the hair follicle with a diameter of app. 200 μ m in the longest direction; scale bar 10 μ m



Matrix-encased *C. acnes* biofilm without obvious attachment to the follicle wall; scale bar 20 μ m

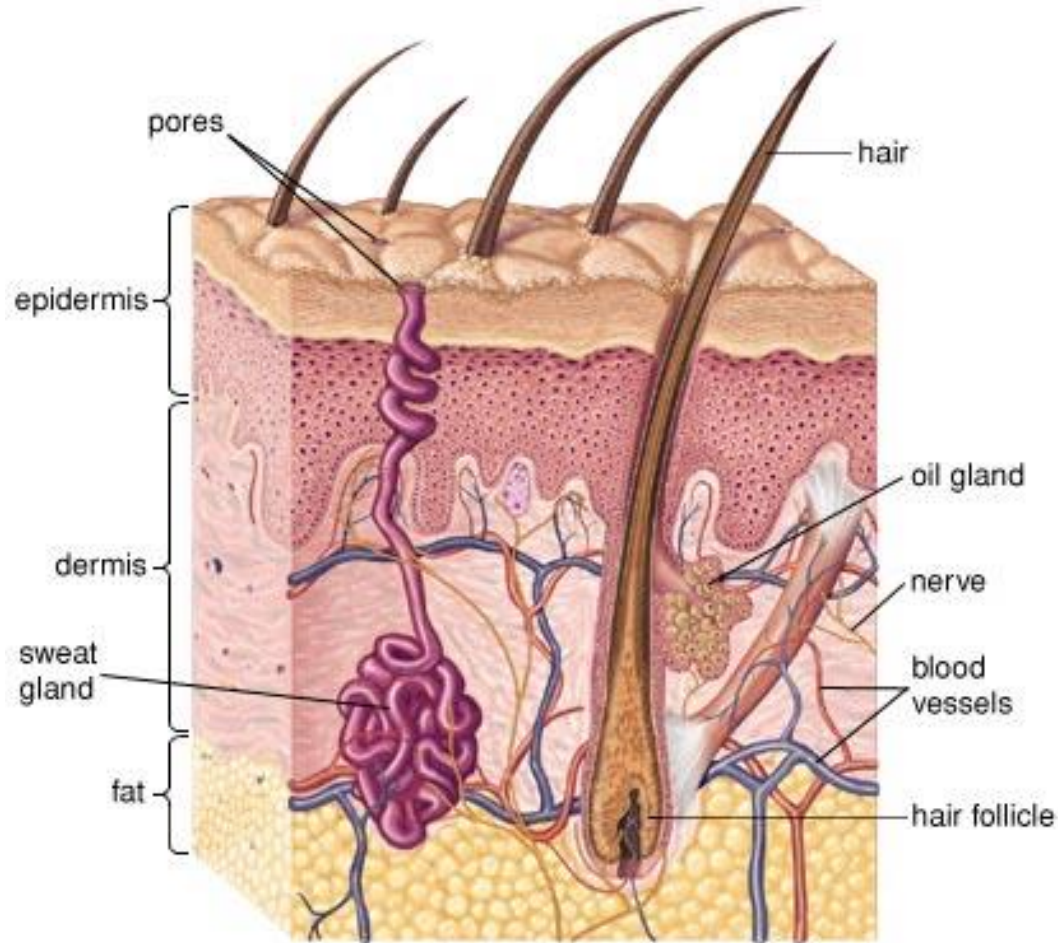


Confocal microscopic images of transversely sectioned skin biopsies highlighting different patterns of *Cutibacterium acnes* colonization in hair follicles; *C. acnes* labelling in green, keratin labelling in red and DAPI labelling of host cells in blue.

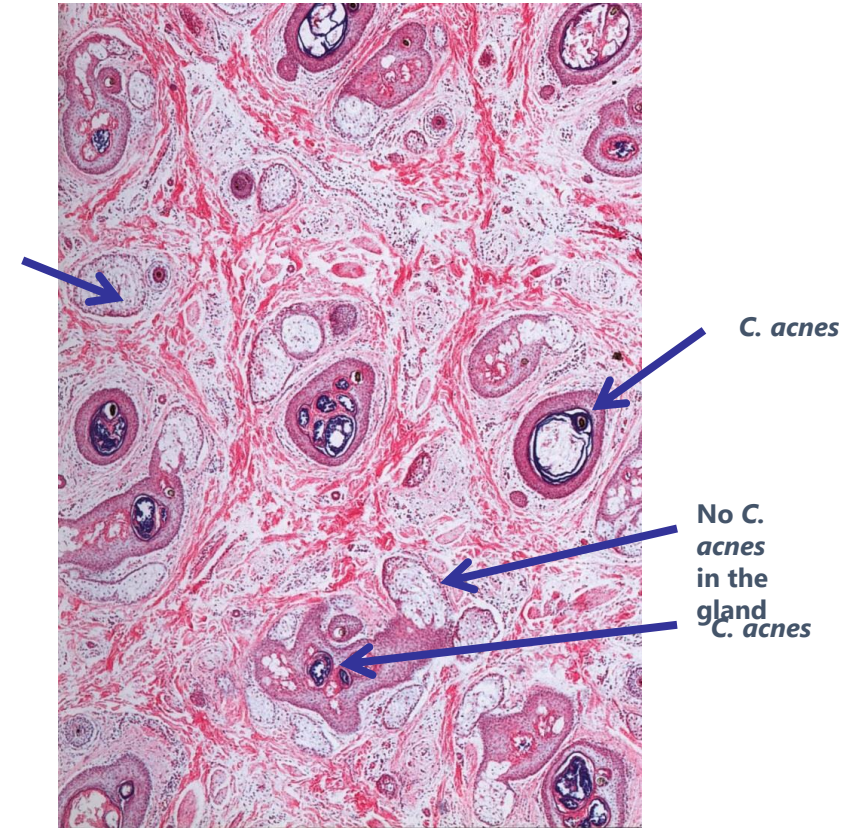
Jahns et. al 2014

EXCLUSIVE INHABITANT

C. acnes in an anaerobic niche on the skin, a microbiome by itself



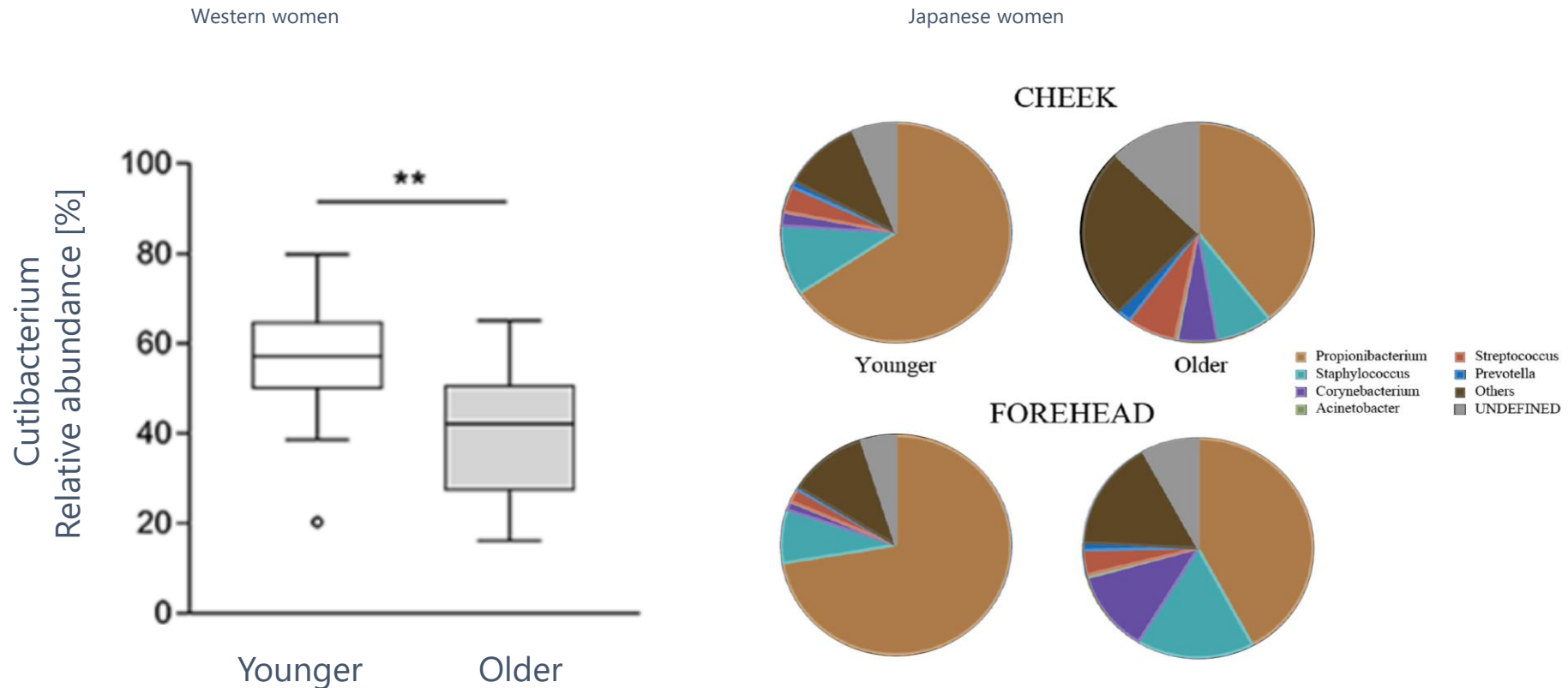
© 2006 Encyclopædia Britannica, Inc.



A horizontal section through acne skin adapted from Plewig & Kligman, Springer

COLONISATION AND SKIN TYPE AGEING

The facial skin microbiome shifts significantly with increasing age in different skin types



Jugé, R., Rouaud-Tinguely, P., Breugnot, J., Servaes, K., Grimaldi, C., Roth, M.-P., Coppin, H., and Closs, B. (2018). Shift in skin microbiota of Western European women across aging. *J Appl Microbiol* 125, 907–916. <http://doi.wiley.com/10.1111/jam.13929>

Shibagaki, N., Suda, W., Clavaud, C., Bastien, P., Takayasu, L., Iioka, E., Kurokawa, R., Yamashita, N., Hattori, Y., Shindo, C., et al. (2017). Aging-related changes in the diversity of women's skin microbiomes associated with oral bacteria. *Scientific Reports* 7, 10567. <https://www.nature.com/articles/s41598-017-10834-9>

COLONISATION AND SKIN TYPE AGEING

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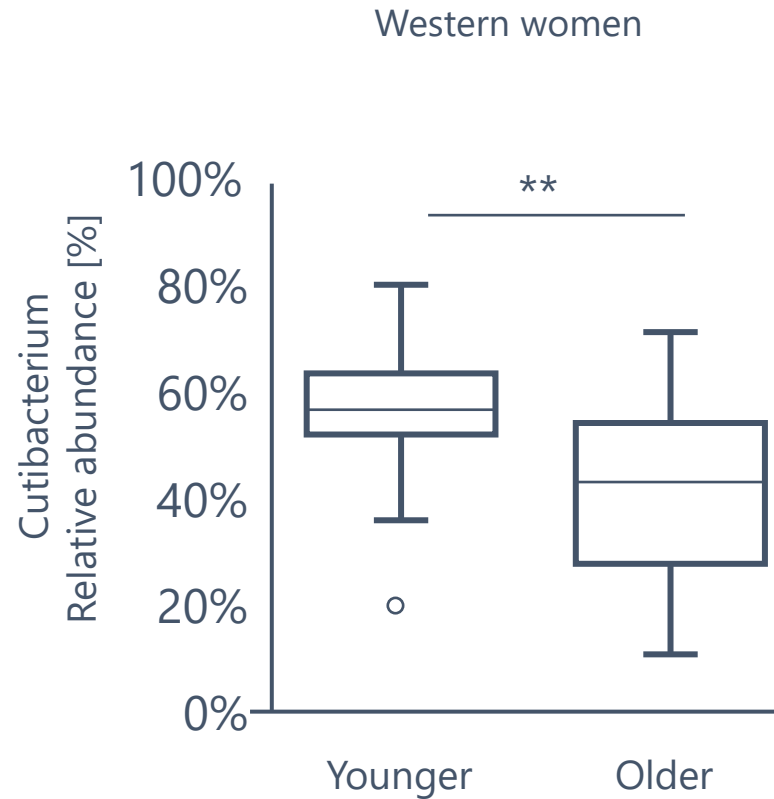
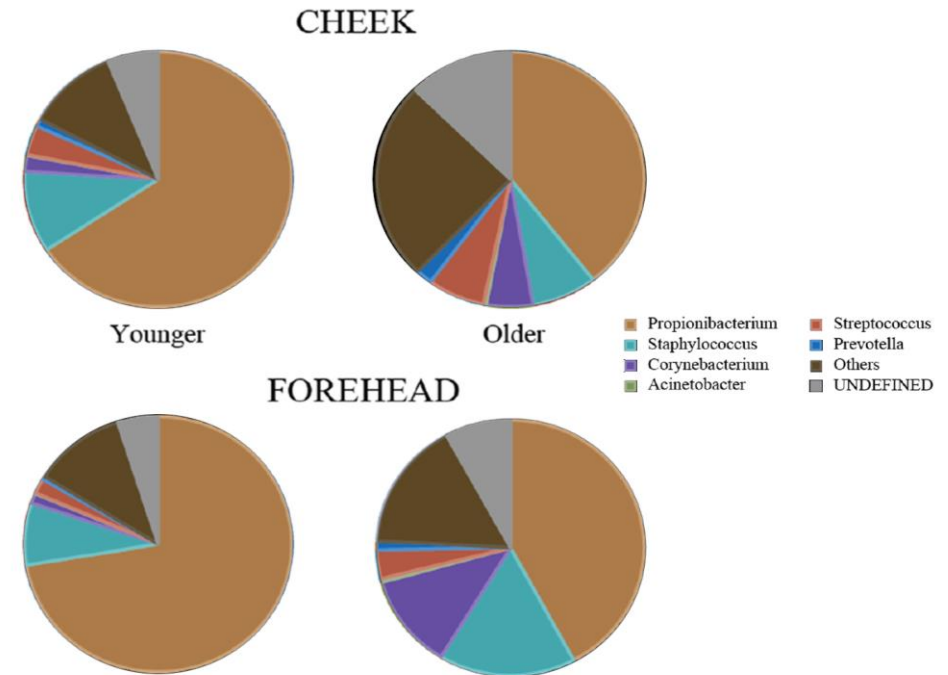


Figure replotted for illustrative purposes from Jugé, R., Rouaud-Tinguely, P., Breugnot, J., Servaes, K., Grimaldi, C., Roth, M.-P., Coppin, H., and Closs, B. (2018). Shift in skin microbiota of Western European women across aging. *J Appl Microbiol* 125, 907–916. <http://doi.wiley.com/10.1111/jam.13929>

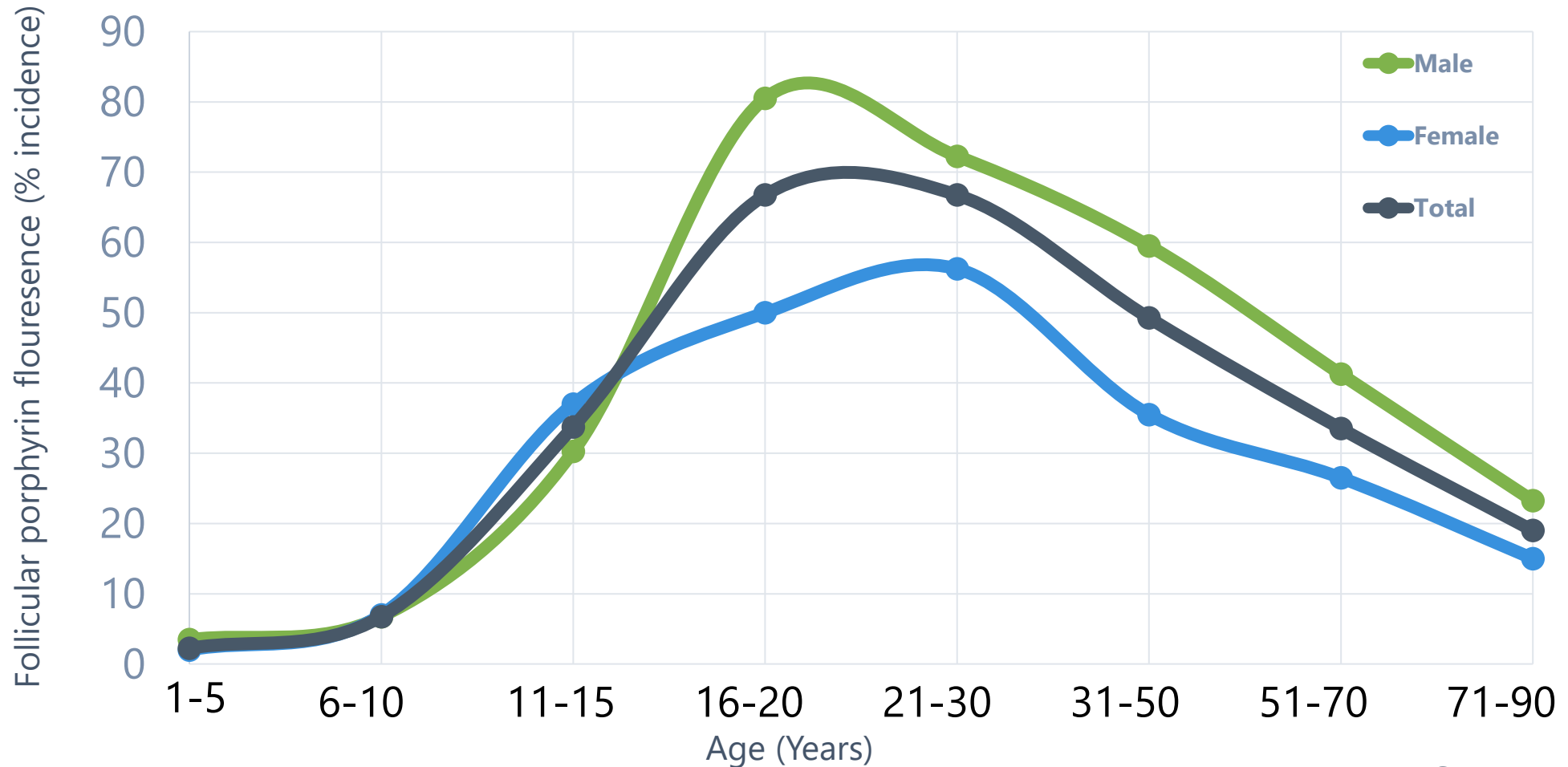
Japanese women



Shibagaki, N., Suda, W., Clavaud, C., Bastien, P., Takayasu, L., Iioka, E., Kurokawa, R., Yamashita, N., Hattori, Y., Shindo, C., et al. (2017). Aging-related changes in the diversity of women's skin microbiomes associated with oral bacteria. *Scientific Reports* 7, 10567. <https://www.nature.com/articles/s41598-017-10834-9>

COLONISATION AND GENDER AGEING

The Cutibacterium population decreases with increasing age in both genders



McGINLEY et al. (1980)

www.sbiomedic.com

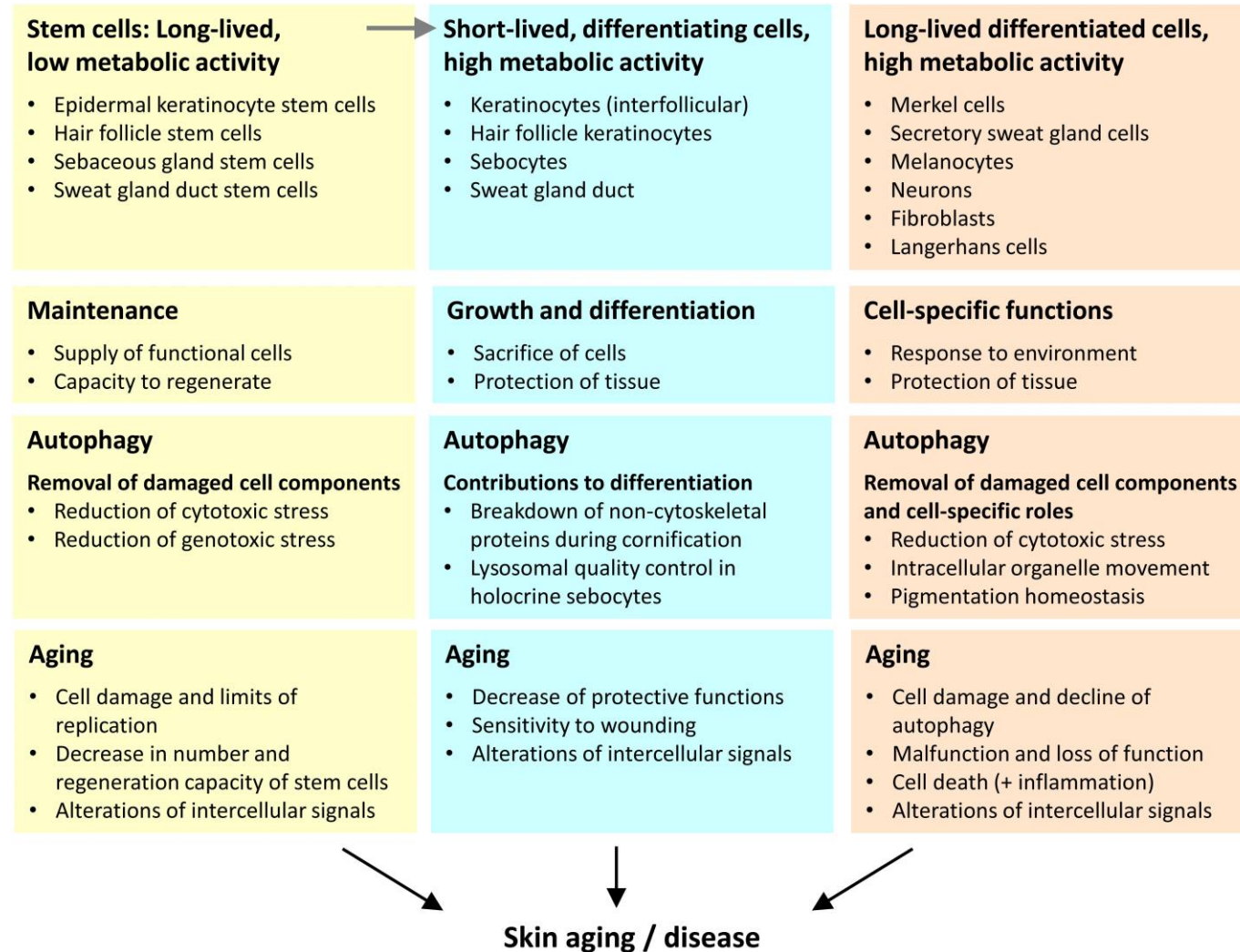
CUTIBACTERIUM DECREASE EFFECT

What we loose when we loose *Cutibacterium acnes*



- Autophagy
- Sebum production
- Antioxidant

AUTOPHAGY A KEY PROCESS IN SKIN HOMEOSTASSIS



C. ACNES INDUCES AUTOPHAGY IN KERATINOCYTES

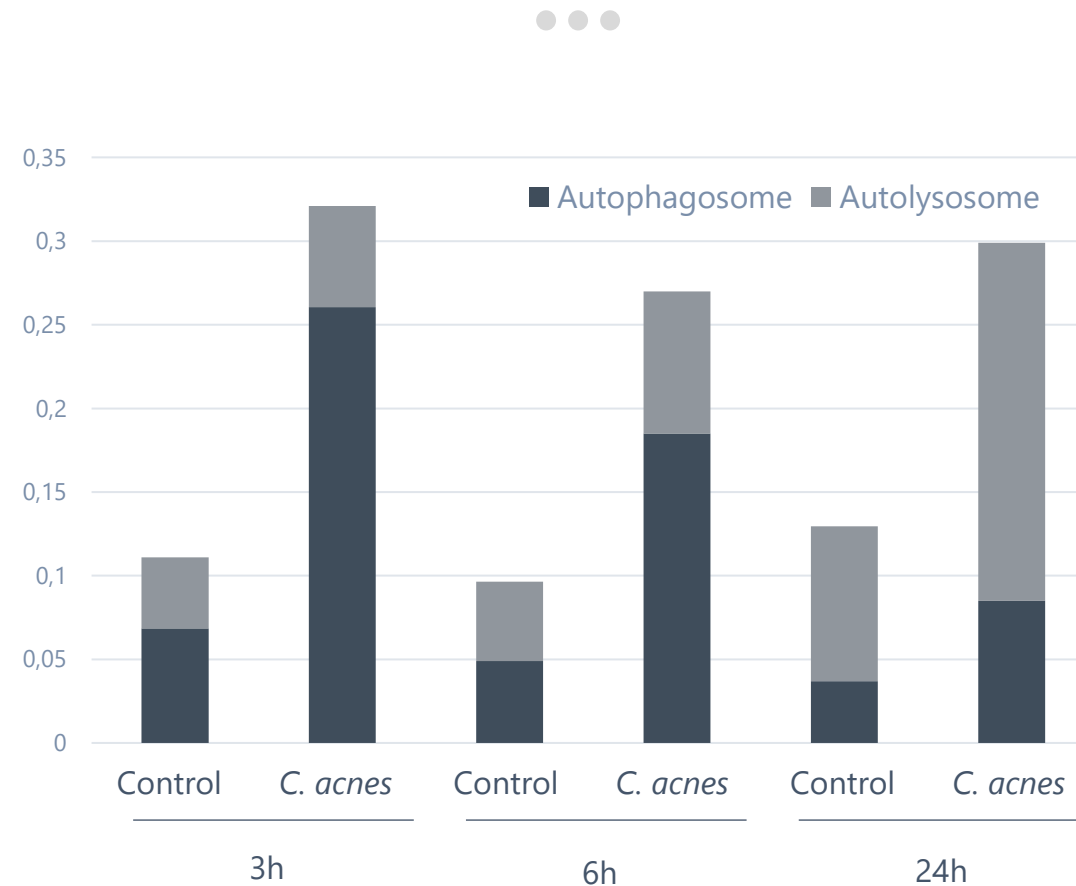
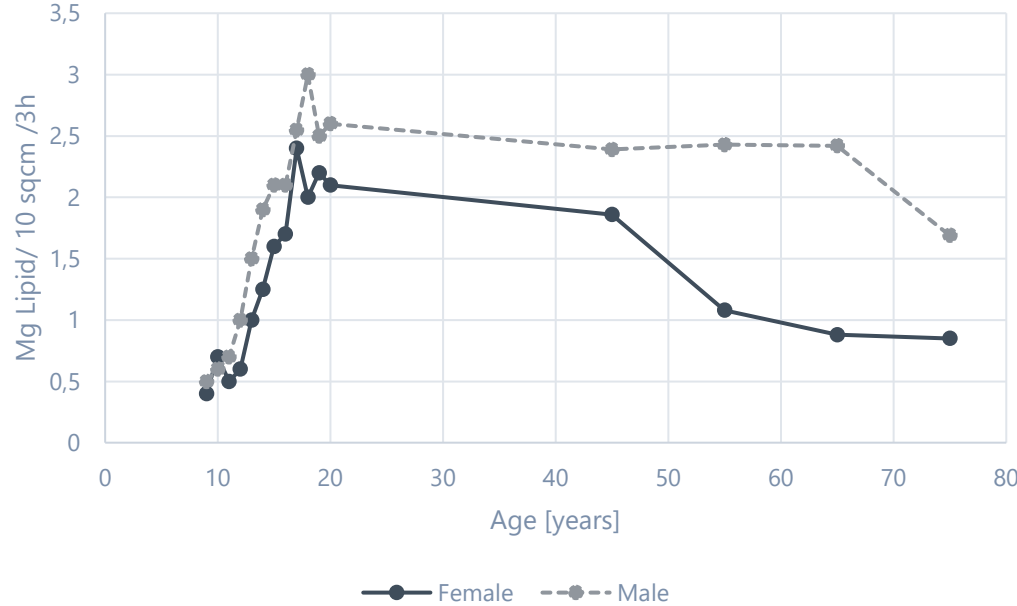


Figure replotted for illustrative purposes from Megyeri, Klára, László Orosz, Szilvia Bolla, Lilla Erdei, Zsolt Rázga, György Seprényi, Edit Urbán, Kornélia Szabó, and Lajos Kemény. 2018. "Propionibacterium Acnes Induces Autophagy in Keratinocytes: Involvement of Multiple Mechanisms." *Journal of Investigative Dermatology* 138 (4): 750–59. <https://doi.org/10.1016/j.jid.2017.11.018>.

AGE-RELATED CHANGES IN SEBACEOUS GLAND ACTIVITY



Strong increase during puberty

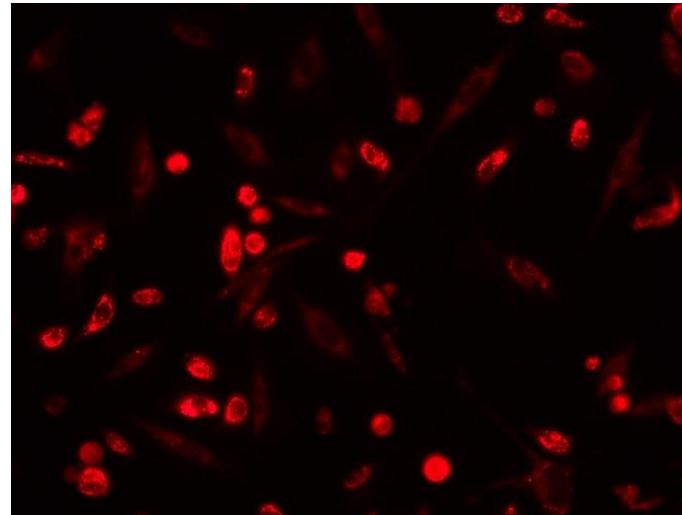
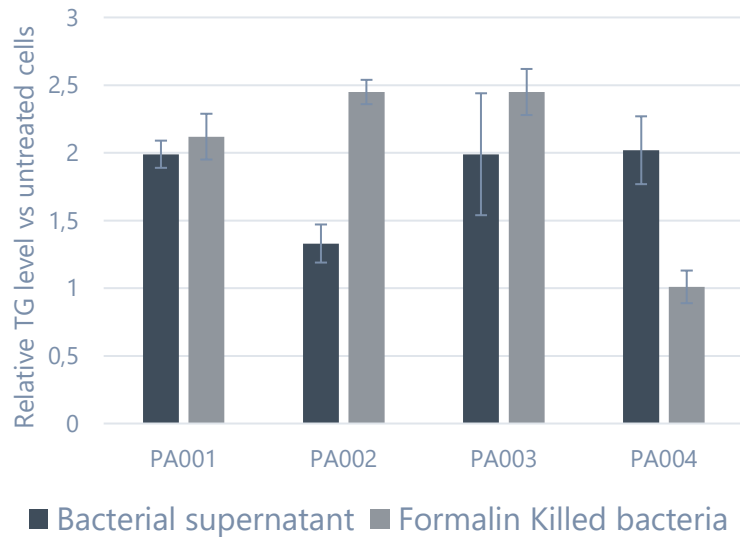


Strong decrease in the later stages of live

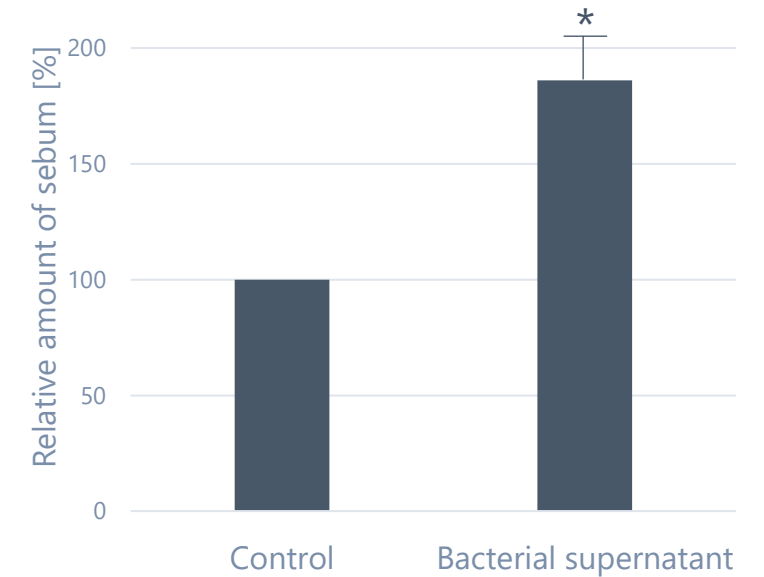
Age	Female			Male		
	No.	Mean	Range	No.	Mean	Range
40-49	31	1,86	0,12-4,8	50	2,39	0,54-5,14
50-59	21	1,08	0,07-2,38	14	2,43	1,05-4,36
60-69	18	0,88	0,22-1,62	14	2,42	0,83-4,95
70-79	12	0,85	0,33-2,19	13	1,69	0,63-3,23

Replotted for illustrative purposes from Pochi, Peter E., John S. Strauss, and Donald T. Downing. 1979. "Age-Related Changes in Sebaceous Gland Activity." *Journal of Investigative Dermatology* 73 (1): 108–11. <https://doi.org/10.1111/1523-1747.ep12532792>.

INVOLVEMENT OF C. ACNES IN AUGMENTATION OF SEBUM PRODUCTION



Lipid production in Sebocytes



Replotted for illustrative purposes from Inuma, Katsuhiro, Takashi Sato, Noriko Akimoto, Norihisa Noguchi, Masanori Sasatsu, Setsuko Nishijima, Ichiro Kurokawa, and Akira Ito. 2009. "Involvement of Propionibacterium Acnes in the Augmentation of Lipogenesis in Hamster Sebaceous Glands in Vivo and in Vitro." *The Journal of Investigative Dermatology* 129 (9): 2113–19. <https://doi.org/10.1038/jid.2009.46>.

Antioxidant



Cutibacterium protect their host from oxidative stress through secreted antioxidant RoxP

HOST INTERACTION OF CUTIBACTERIUM

Proteins produced by *C. acnes* in the follicle and in vitro



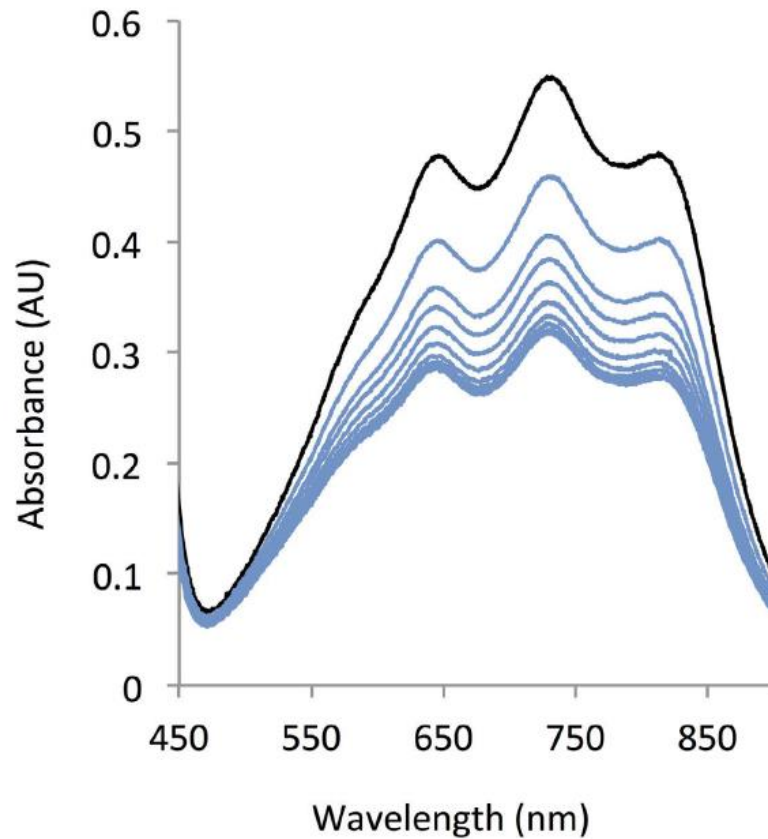
The 20 most abundant secreted proteins.



Protein	Accession (gi)	MW (kDa)	Function
Protein PPA1939	50843388	17	Unknown
Adhesion	50843565	42	Adhesion
cAMP factor	50842175	29	Digestion
Protein PPA2239	50843674	41	Digestion
Protein PPA2271	50843708	52	Digestion
Endoglycoceramidase	50842131	57	Digestion
Protein PPA1746	50843206	22	Unknown
NPL/P60 protein	50842209	41	Digestion
Cell wall hydrolase	50843410	43	Digestion
Protein PPA1745	50843205	90	Digestion
cAMP factor	50842820	30	Digestion
Chaperone GroEL	50841936	57	Protein folding
Triacylglycerol lipase	50843543	36	Digestion
Protein PPA0533	50842017	20	Unknown
co-chaperonin GroES	50843233	11	Protein folding
Endoglycoceramidase	50843544	54	Digestion
Fine tangled pili	50843572	19	Mobility
Lipase/acylhydrolase	50843480	30	Digestion
Regulatory protein	50842205	39	Translation
Protein PPA1715	50843175	49	Unknown

A NOVEL ENZYME WITH ANTIOXIDANT CAPACITY

PPA 1939 the most abundant secreted protein by *C. acnes* is an antioxidant

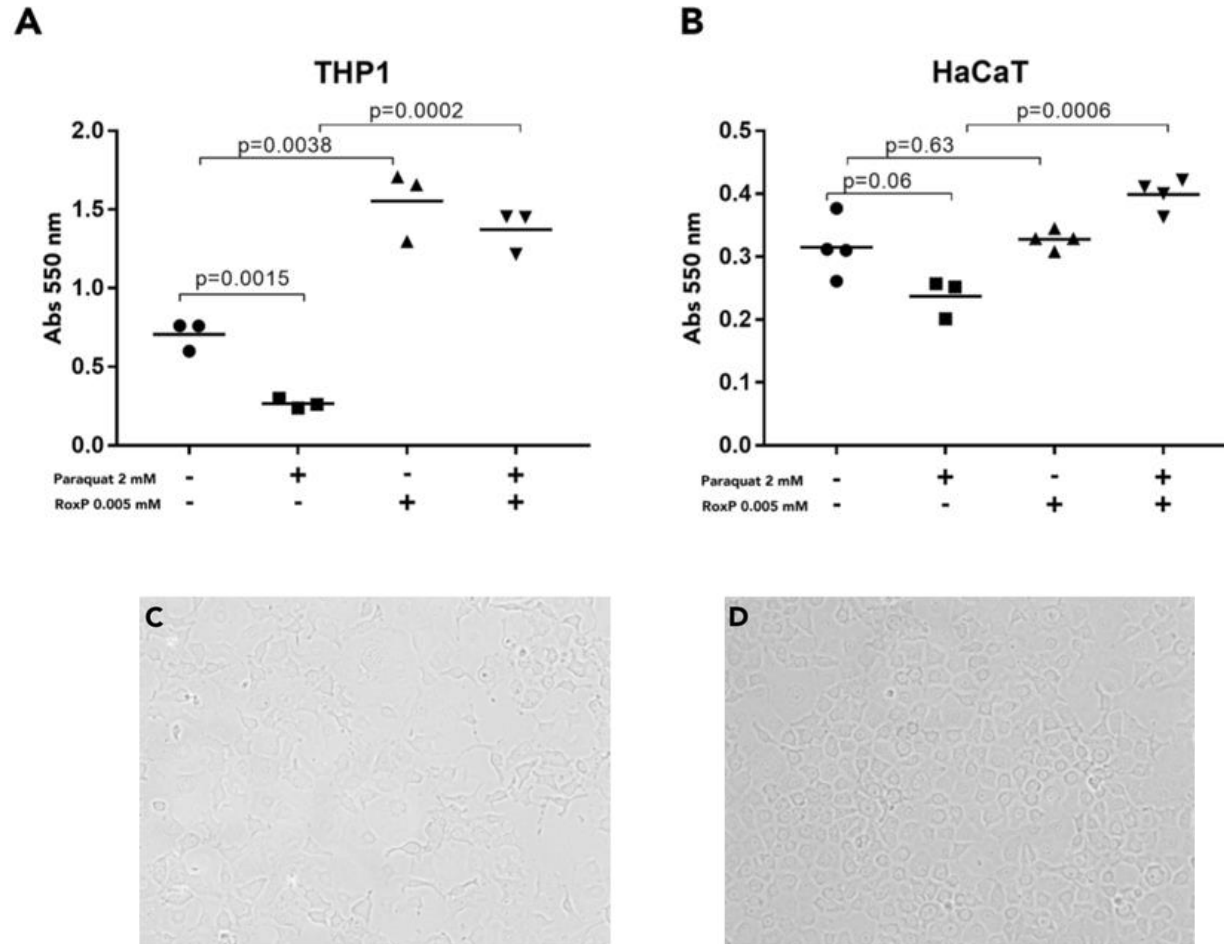


(min)	% inhibition
0	0,0%
2	16,4%
4	26,1%
6	29,8%
8	33,9%
10	37,0%
12	39,5%
14	41,0%
16	41,6%
18	42,3%

Allhorn, M., Arve, S., Brüggemann, H., and Lood, R. (2016). A novel enzyme with antioxidant capacity produced by the ubiquitous skin colonizer *Propionibacterium acnes*. *Sci Rep* 6.

IN VITRO SKIN DAMAGE

RoxP protects human cells from oxidative damage *in vitro*



Andersson et al. 2019

CUTIBACTERIUM AND AGEING SKIN

Cutibacterium amounts are reduced with increasing age.



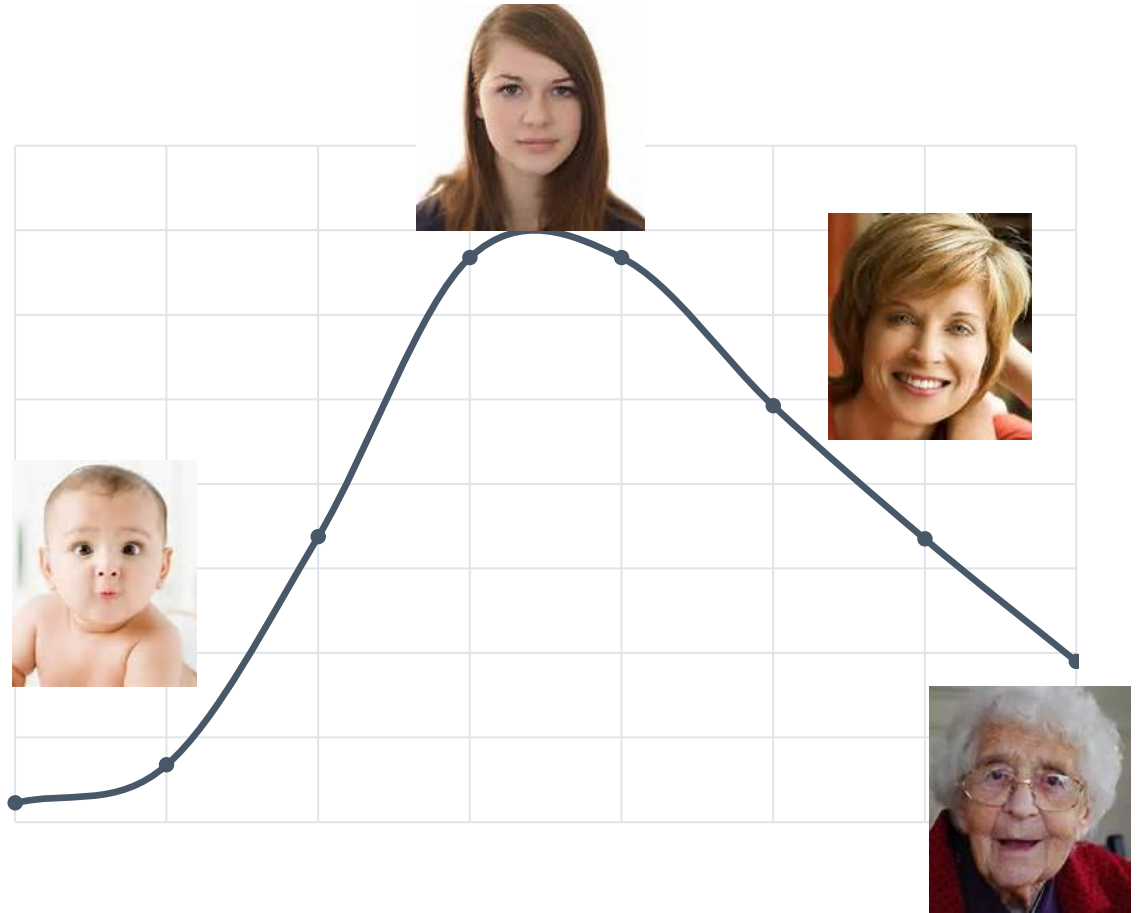
The amount of Cutibacteria declines with age

With Cutibacterium decline, the amount of protective **antioxidant decreases**

With Cutibacterium decline, the amount of **Sebum decreases**

With Cutibacterium decline, the amount of **Autophagy decreases**

Amount of Cutibacterium on the facial skin



CONCLUSION:

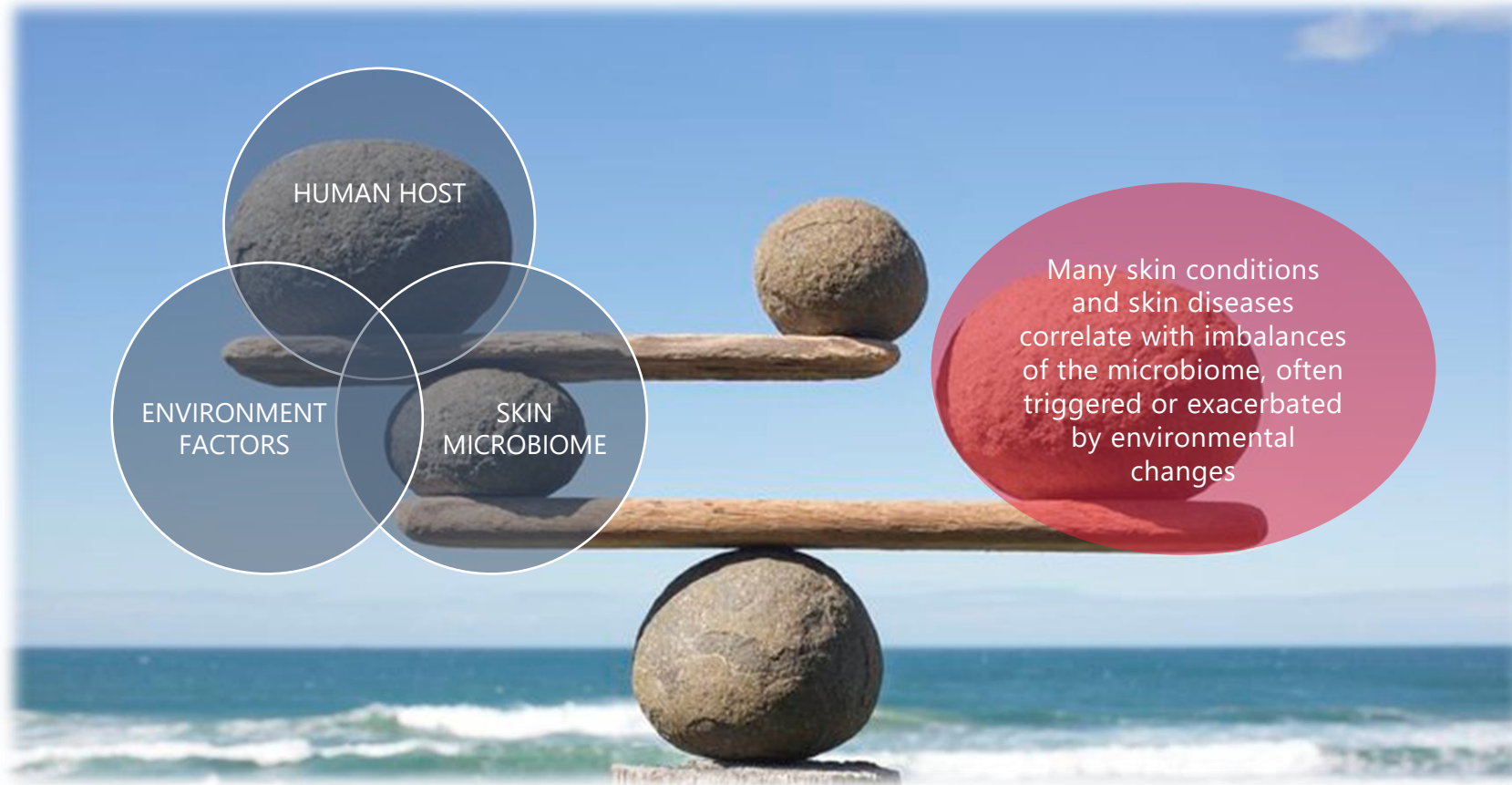
CUTIBACTERIUM ACNES
THE KEY TO THE FACIAL MICROBIOME

&

CUTIBACTERIUM ACNES
THE KEY TO SKIN AGEING

SYMBIOSIS INTO TECHNOLOGY

Balance is about the distribution of elements. S-Biomedic is pioneering at the skin-microbiome interface to balance the system



S-Biomedic develops microbiome-based active ingredients such as anti-ageing metabolites to modulate the skin microbiome and establish healthy skin

ACKNOWLEDGEMENT

to founders, senior team and top positioned advisors together with many more people who support S-Biomedic



VERONIKA OUDOVA

More than 10 years of business, management and startup experience.

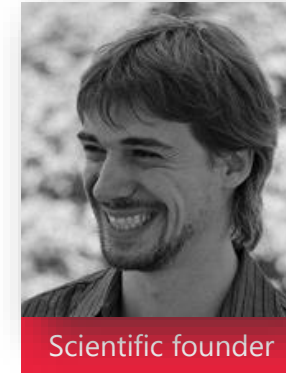
CEO



BERNI PÄTZOLD, PHD

PhD in synthetic biology, expert in designing bacteria as living pills.

CSO



MARC GÜELL, PHD

Tenure track professor UPF, Wyss Fellow at Harvard University, expert in CRISPR gene editing.

Scientific founder



W. CARPENTIER, PHD



CCO



SITARA PANIKAR



Head Marketing



LIEVE DECLERCQ, PHD

ESTÉE LAUDER

Health & Beauty



PROF. DR. GOLLNICK



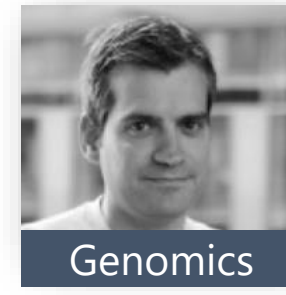
Acne KOL



DIRK GEVERS, PHD



Microbiome



PROF. TONI GABALDON



Genomics



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THE POWER OF YOUR SKIN MICROBIOME

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