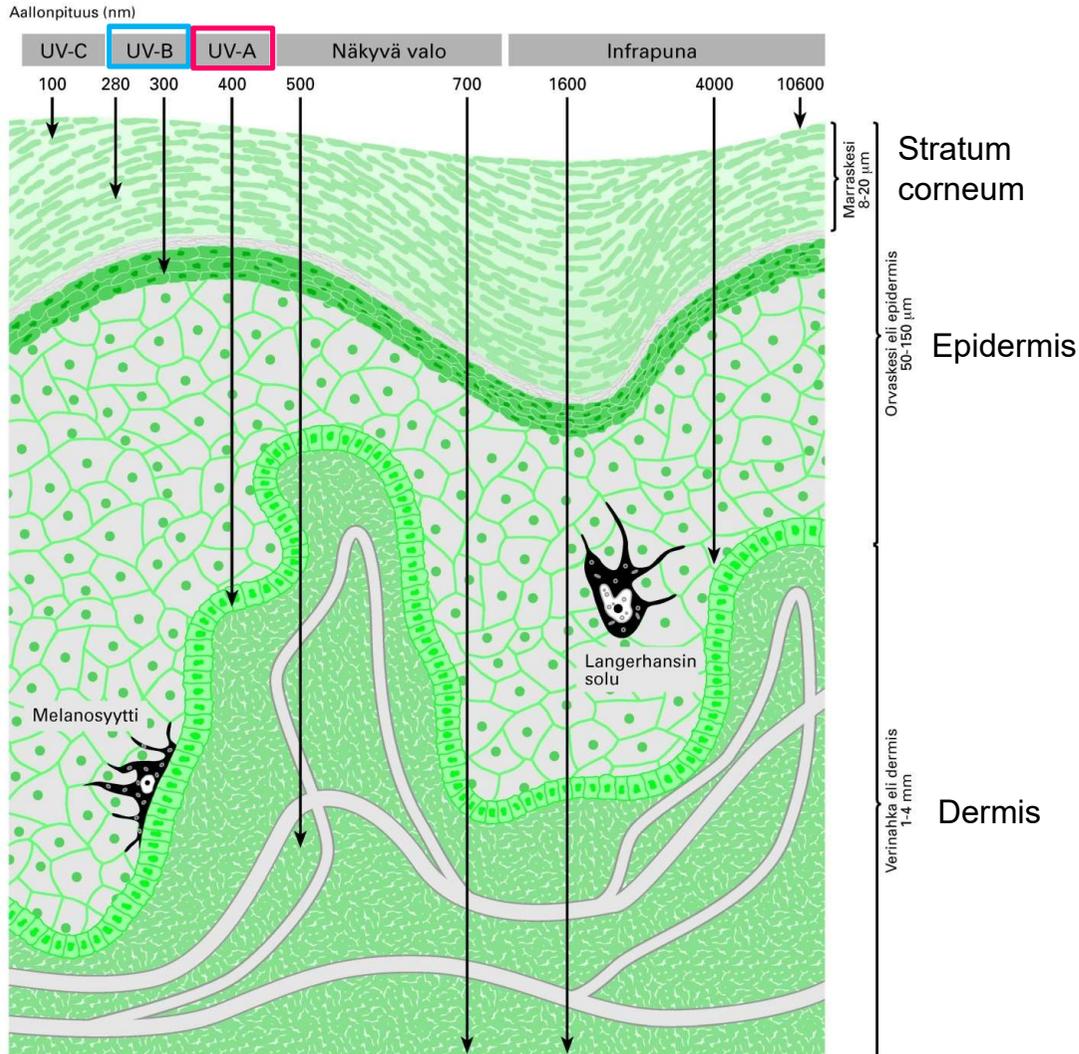




The health effects derived from UV radiation and sunbed use

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UVB: 280-320 nm

- Skin tanning, erythema formation (snow blindness in eye)
- A Full Carcinogen: Initiator and promotor
- Causes DNA damage directly -> leads to UV-signature mutations (CC to TT transitions)
- Immunosuppressive
- Vitamin D synthesis

UVA: 320- 400 nm

- Carcinogenic: DNA damage mainly via reactive oxygen species (ROS)
- Photoaging
- Immunosuppressive

UV radiation as a risk factor for skin cancer formation

- Skin cancer incidence has increased substantially over the past decades and the role of UV radiation in the etiology of skin cancer is well established
- Basal cell carcinoma (BCC), and especially Squamous cell carcinoma (SCC), are related to the cumulative, lifetime UV exposure
- Both types are prevalent at the elderly age groups on the sun exposed areas

Basal cell carcinoma (8528 in 2016)



Squamous cell carcinoma (1719 in 2016)



Malignant melanoma is one of the fastest increasing cancer in incidence in the western world

- Associated strongly with intermittent UV exposure (history of sunburns), rather than chronic exposure, with genetically susceptible individuals
- Intermittent exposure in childhood and adolescence has an important role, although the adult exposure contributes as well
- Prevalent among younger adults as compared to BCC and SCC



- There were 1947 melanomas in Finland in 2016
- There were 212 melanoma deaths in Finland in 2016

Photography by Dr. Olli Saksela

Sunbeds



Sunbeds now and then

- Sunbeds were first introduced to the market in the late 1970's¹
 - Mercury lamps emitted mainly UVB wavelengths and even some UVC
 - Mainly used at homes
- In 1980's indoor tanning became more popular in beauty salons¹
 - Lamps emitted 99% of UVA and 1% of UVB
- Nowadays sunbeds contain as much UVB as in the sunlight, but **considerably more UVA as compared to the sun**^{2,3}
- **Repeated exposure to large amounts of UVA** in relatively short periods (10-20 mins per tanning session) **constitutes a new experience for skin**

Sunbed power indicated by UV index*

- Sun, Helsinki Finland, December 0,1
- Sun, Helsinki Finland, Mid-Summer 6-7
- Sun, Mediterranean, Mid-Summer 11
- Sunbeds in EU 12
- Sunbeds out of EU even up to 24

Sunbed use – who and why

- Indoor tanning is a widespread practice in most western countries, particularly in Northern Europe and the USA
- The typical sunbed user is a female, between 17-35 y old (Schneider and Krämer, 2010)

| | <u>1997*</u> | <u>2011*</u> | <u>2016*</u> 1 st reason | <u>2016*</u> 2 nd reason |
|-------------------------|--------------|--------------|--|--|
| • Cosmetic Tanning | 30% | 44% | 76% | - |
| • Tanning before a trip | 36% | 28% | 6% | 18% |
| • Doctor's referral | 4% | 5 % | 2% | 2% |
| • 'Self-medication' | 8% | 4 % | 1% | 28% |
| • Mood uplift | 11% | 3 % | - | 30% |
| • General health uplift | - | 2% | 14% | 7% |

Tan – is it protective?



Yes and no....

- Constitutive epidermal melanin seems to be very effective in darker skin types to protect the underlying cells from UV radiation^{1,2}
 - Provides **sun protection factor (SPF) ~13**
 - Pretty good 'real' protection for skin cells in UV-independent process
- Fair skin types react to UV radiation by facultative pigmentation, i.e tanning
 - Provides **sun protection factor (SPF) ~ 2-3**

Sunbed-derived tanning – is it worth it?

- UVA-rich tanning lamps have previously been promoted as ‘damage-free’, however this message could be a deceptive one
 - UVA does not increase melanin production or redistribution in epidermis, mainly photo-oxidation (darkening) of the existing tan
 - UVA-induced tan offers no photo-protection against UV exposure¹
- UVA is a possible carcinogen especially for melanoma formation^{2,3}
 - Several animal models (fish, opossum, mice) suggest that UVA might have a role in melanomagenesis
- Sunbed is not an optimal way to ensure vitamin D synthesis due to the unnaturally large amount of UVA radiation that comes along

Sunbed use and skin cancer

- International Agency for Research on Cancer (IARC) classified artificial UV tanning devices as carcinogenic to humans
 - A 'hall mark' meta-analysis found a **significant increase in risk of malignant melanoma** , especially if sunbed use started before age of 35 (IARC 2006)
 - Epidemiological data published after the original IARC report strengthens the link between MM and artificial tanning ¹⁻³
 - 7% of malignant melanomas (MM) in women, and 4% of MM in men, has been estimated to be related to the sunbed use⁴
 - Sunbed use has been also linked to SCC and BCC formation, especially if sunbed use started before age of 25 years⁵
- Many countries have passed local/statewide laws, that restrict the sunbed use by age (18 y) to protect young people from the UV-derived health hazards

Sunbed addiction

Several studies have suggested that tanning behavior exhibits signs of psychologic and physiologic dependence

- First postulated in 1983, when UVA (but not visible light) increased a elevation of plasma endogenous opioid levels¹
- Surveys studies have reported of relaxation, pain relief and positive mood effects^{2,3}
- In an experimental sham study (blinded trial), frequent solarium users seemed to sense with their skin the true solarium from a sham device⁴
- A subsequent study in 2006 showed that an opioid blockade (by naltrexone) induced withdrawal symptoms for frequent tanners'⁵

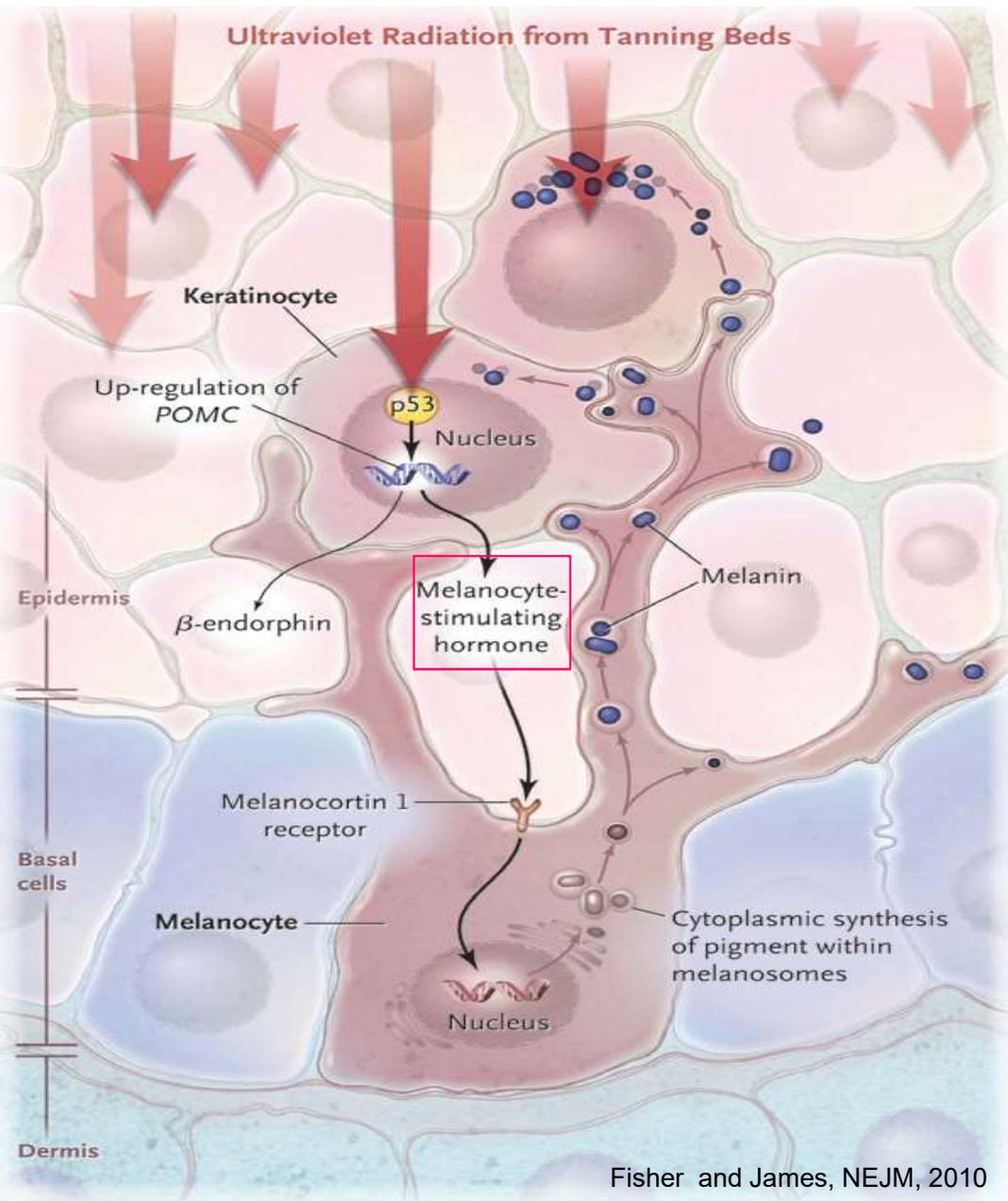
1 Levins et al. Lancet 1983; 2:166

2 Nolan and Feldman. Dermatol Clin 2009; 29: 109-112

3 Kaur et al. Photochem Photobiol Photodermatol 2005

4 Feldman et al. J Am Acad Dermatol 2004; 51(1): 45-51

5 Kaur et al. J Am Acad Dermatol 2006; 54(4): 709-711



Mechanism for action – a hypothesis

- UV-derived DNA damage activates of tumor suppressor protein p53 (guardian of genome) in keratinocytes
- p53 stimulates the transcription of pro-opiomelanocortin (POMC)
- Cleavage products of POMC are Melanocyte-Stimulating Hormone (MSH- α) and β -endorphin
- MSH activates the melanin synthesis in melanocytes (tanning)
- β -endorphin expression may be in response in reinforcing UV-seeking behavior of heavy tanners

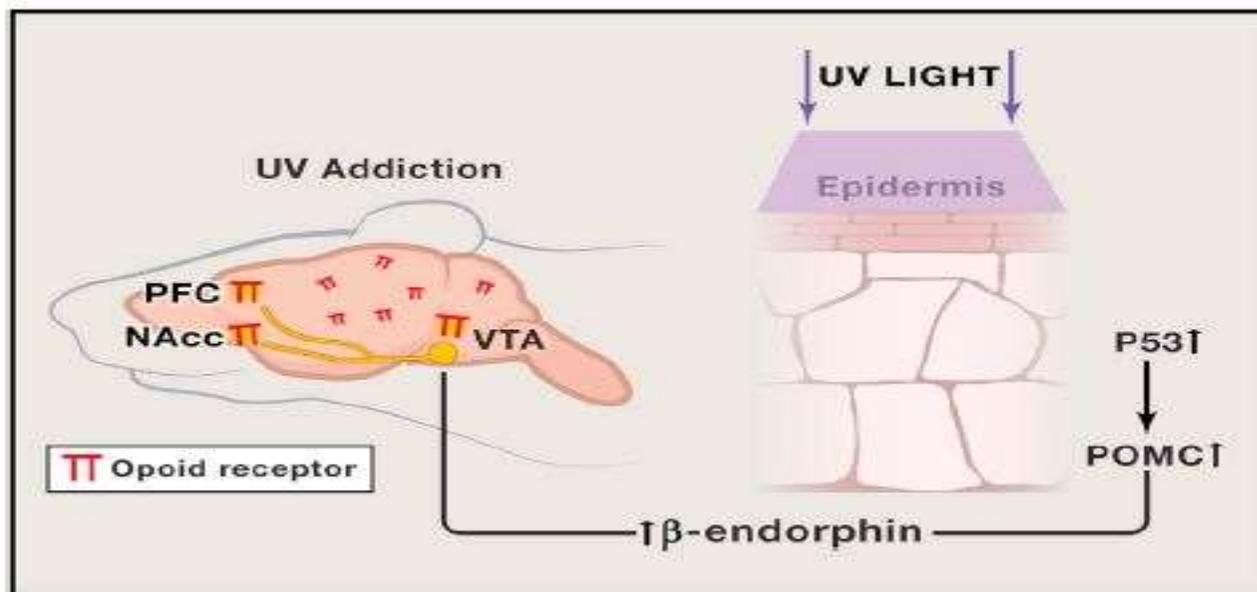
Fisher and James, NEJM, 2010; 363:903-903

Fell et al. Cell, 2014; 157(7): 1527-1534

Skobowiat C, Slominski AT. J Invest Dermatol. 2015;135:1638-1648

Jussila et al. J Photochem Photobiol B: Biol, 2016; 155: 104-108

Working model of endogenous opioid dependence caused by chronic UV exposure



UV induces p53 signalling in keratinocytes, increasing the synthesis of POMC peptide and the concomitant β -Endorphin in the skin, leading eventually to the elevated plasma levels of β -Endorphin

Sustained levels of plasma β -Endorphin, increase signaling at opioid receptors in the central nervous system, producing the endogenous opioid -dependent state

Tejeda and Bonci, Cell, 2014; 157: 1500-1501

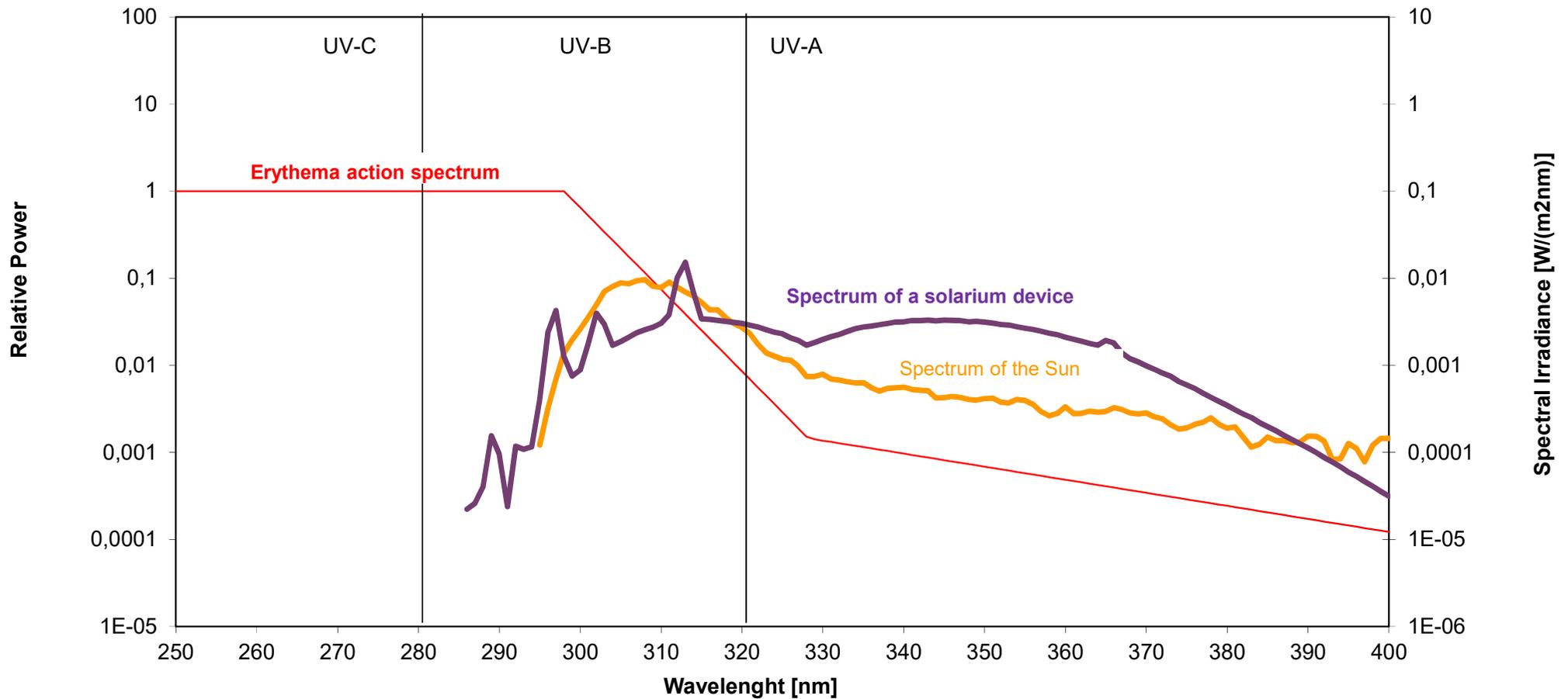
➔ The possible mechanism for sun-seeking behavior

“Take home messages”

- There is no safe tan from natural or artificial UV-sources
- Sunbed use has been linked with skin cancer formation, especially with melanoma
- Ultraviolet tanning can be addictive through β -Endorphin secretion from skin cells after UV exposure
- Solarium use restrictions aim to protect adolescents from UV derived health problems and also to minimize health care expenses for the long run

Extras

Typical Spectrum of solarium device in Finland



- The effect of UV radiation on skin depends on its wavelength
- The action spectrum depicts the waveband-dependency of the irradiation

Legislation changes regarding sunbed use

- Many countries have passed local/statewide laws, that restrict the sunbed use by age (18 y) to protect young people from the UV-derived health hazards
 - Austria, Belgium, [Canada \(2018\)](#), Chile, France, [Finland \(2012\)](#), Germany, Iceland, Ireland, Italy, Israel, Latvia, Lithuania, the Netherlands, Norway, Portugal, Spain, [Sweden \(2018\)](#), Slovakia, Scotland, Wales and North-Ireland, some states in the USA
- Brazil (since 2009) and Australia (since 2016) have implemented an outright ban of sunbed trade and use for cosmetic purposes

β -endorphin and UV exposure

- In humans, endogenous β -Endorphin is linked with feelings of euphoria, for example in the ‘*runners high*’
 - Chronic exposure to opioids results in tolerance, requiring an increase in the dose, leading to the physical dependence (addiction)
- Studies^{1, 2} *in vivo* on mice have shown UV-B to be capable of inducing β -endorphin expression in the skin (as show in the previous slide) leading to the elevated plasma levels, even to the point of developing addictive behaviour towards UVR
 - Withdrawal symptoms after naloxone administration (anxiety, shaking)
- In the recent study³, β -Endorphin expression was increased *in vivo* in human skin biopsy samples taken at 24 h after UV-B exposure