



# ScarCon ETRS 2018

Linking knowledge to heal scars

**MAY 31 - JUNE 2, 2018**  
**HOTEL OKURA, AMSTERDAM**  
[www.scarconetrs2018.org](http://www.scarconetrs2018.org)

Fibrosis

Wound care

Scar management



Scars

Wound

Fibrosis

Scar

Management



# Белок Klotho

Enhances cardiovascular function

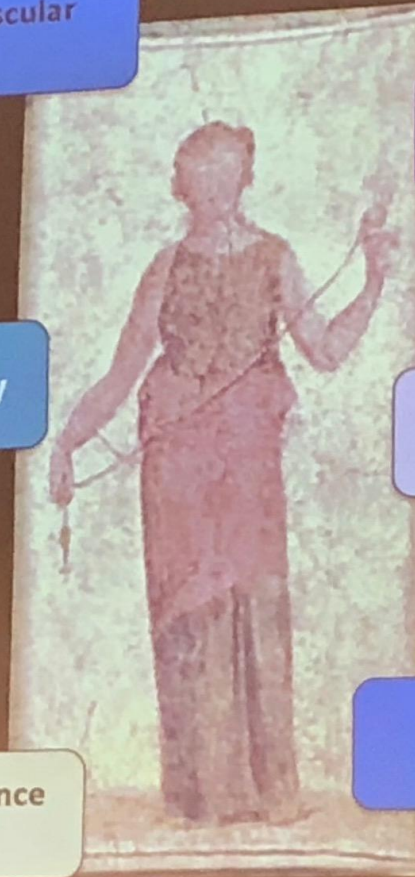
Preserves brain health

Promotes tissue vascularity

Enhances stem cell function

Increases cellular resistance to stress

Decreased risk of cancer





Греческие богини  
судьбы:

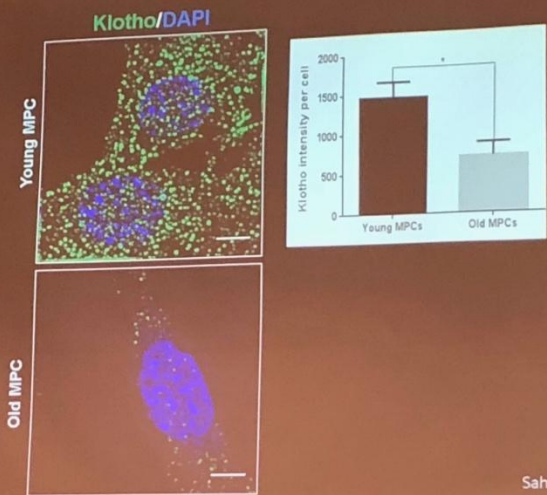
**Лахесис** – дающая  
жребий

**Клото** – прядущая  
НИТЬ ЖИЗНИ

**Атропос** –  
«неотвратимая»,  
обрезающая нить



Klotho is highly expressed in young muscle stem cells, but expression is attenuated with age

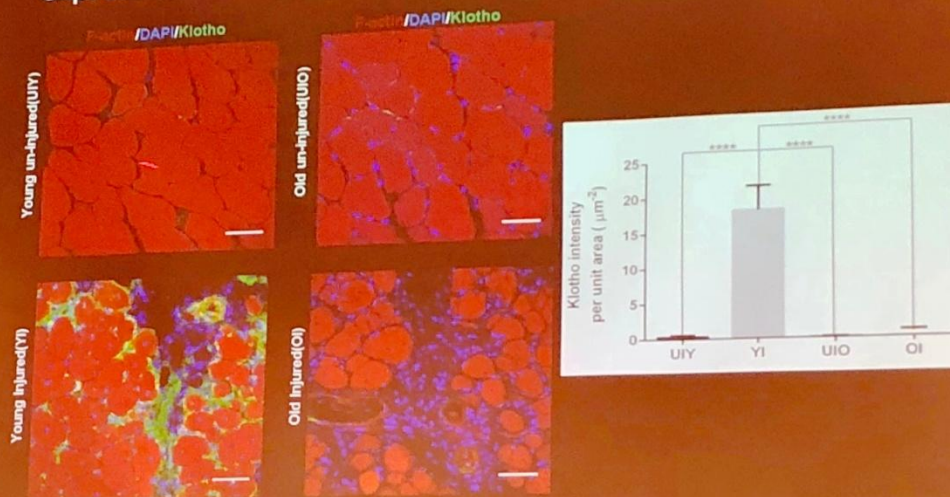


Sahu et al, under

Экспрессия белка Клото в тканях молодых и старых мышей до и после повреждения мышцы.



Klotho is highly expressed in young injured muscle, but expression is attenuated in aging



Sahu et al, under review

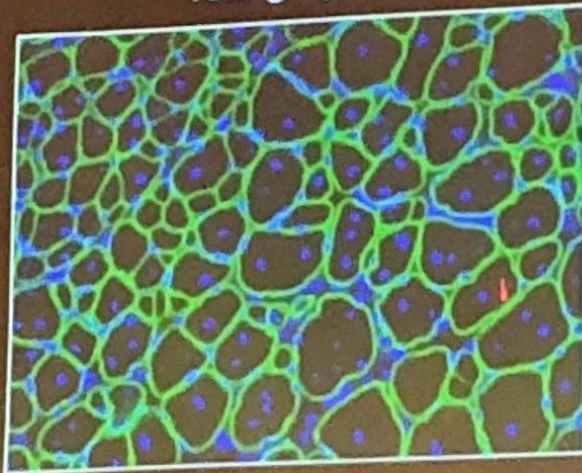
Высокая экспрессия белка Клото в мышечных клетках молодых мышей и ослабление экспрессии в клетках возрастных мышей



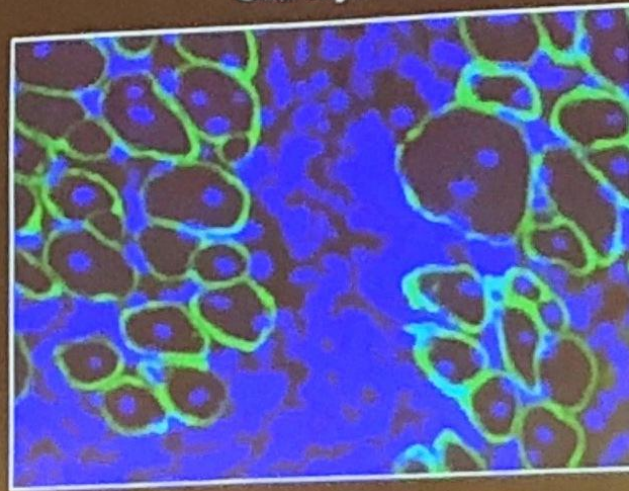
# Уменьшение способности к регенерации и увеличение фиброза мышц у возрастной мыши

Aging results in a decreased skeletal muscle regenerative capacity and increased fibrosis after injury

Young injured



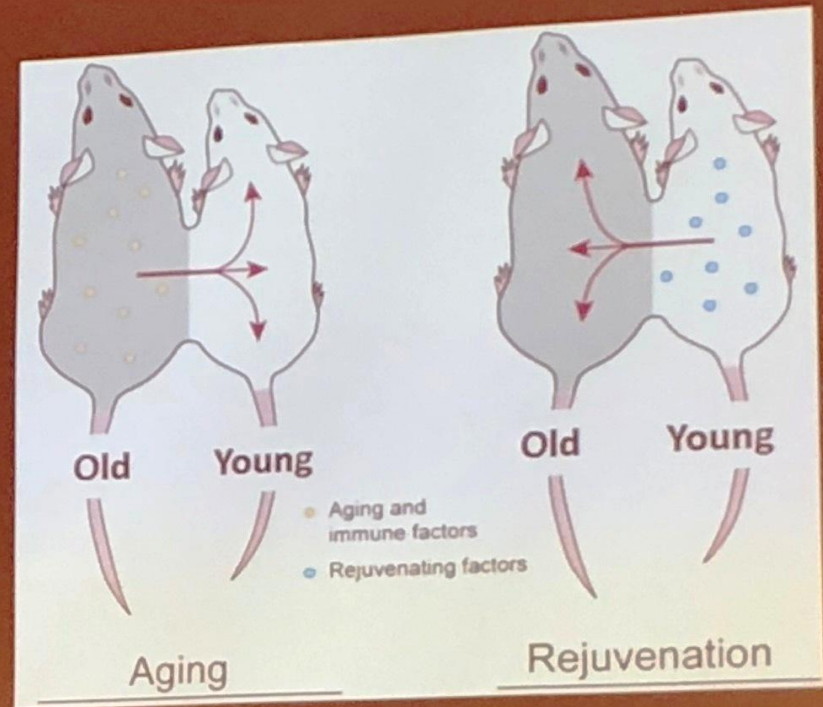
Old injured



Laminin DAPI

# Эксперимент

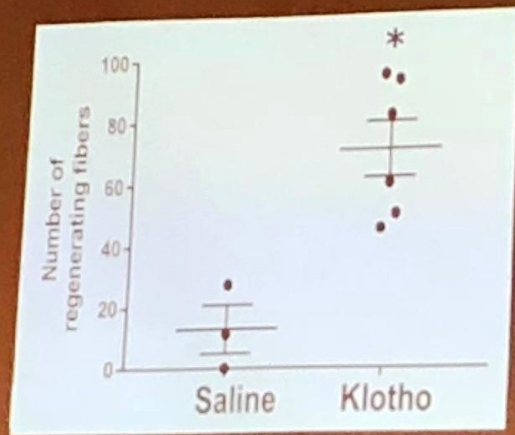
The stem cell niche is composed of soluble factors that provide cues for stem cell-mediated regeneration.



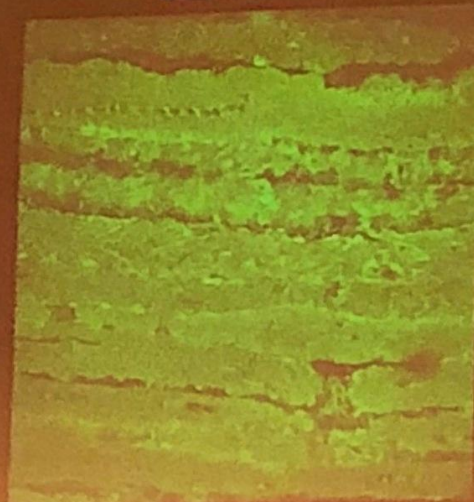


# Системное увеличение Клото вызвало усиление регенерации у возрастной мыши

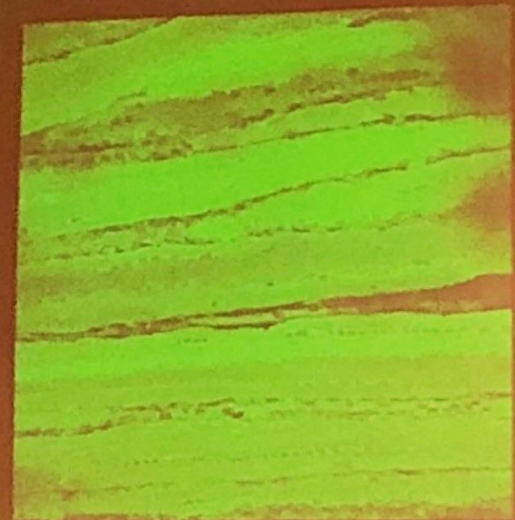
Systemic Klotho supplementation enhances the regeneration of aged mice



Old Control



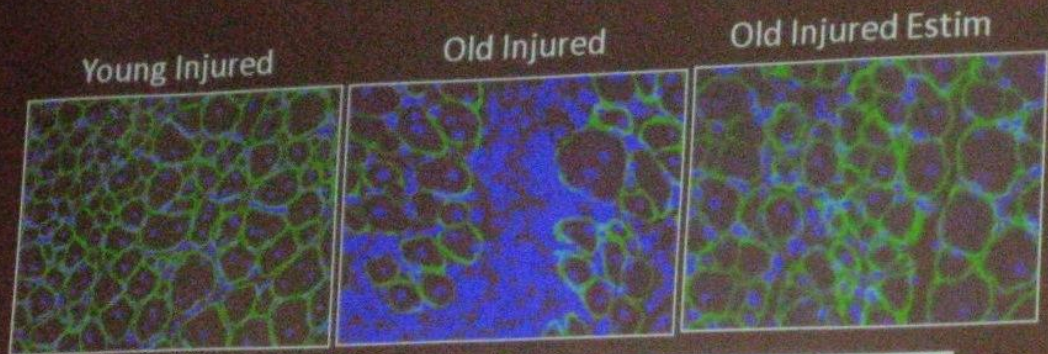
Klotho Osmotic Pump



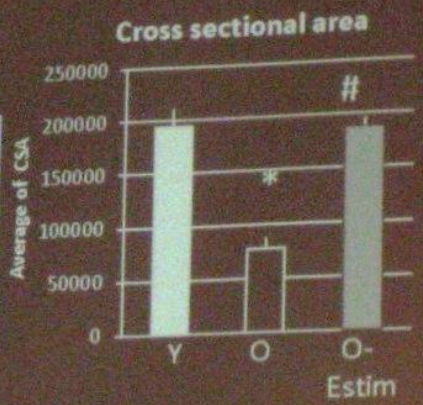


# Оценка увеличения регенерации миофибрилл и функционального восстановления после травмы

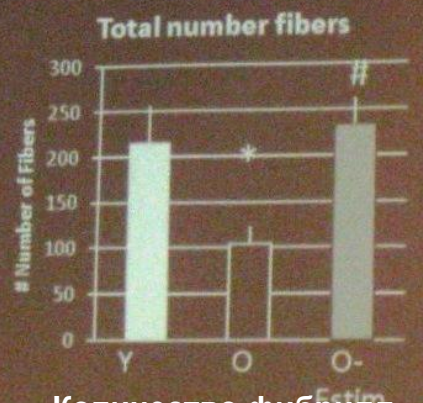
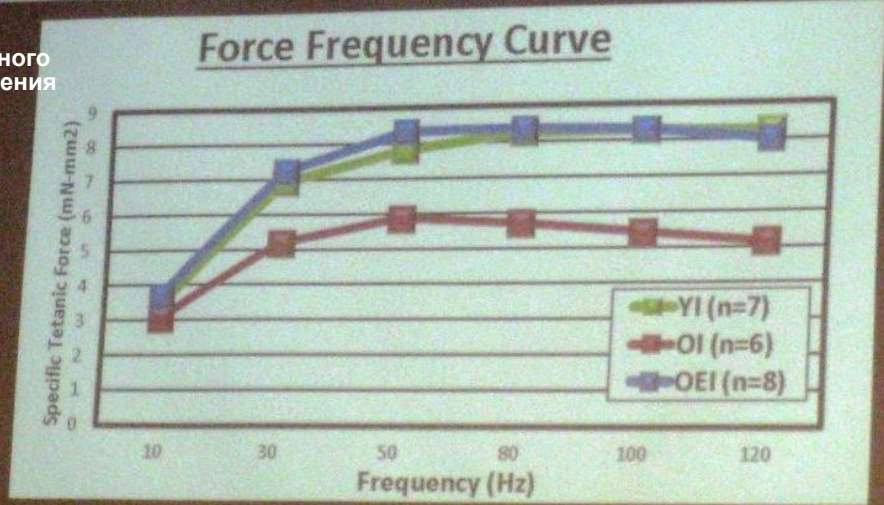
Estim enhances myofiber regeneration and functional recovery after injury in aged muscle



- площадь поперечного сечения



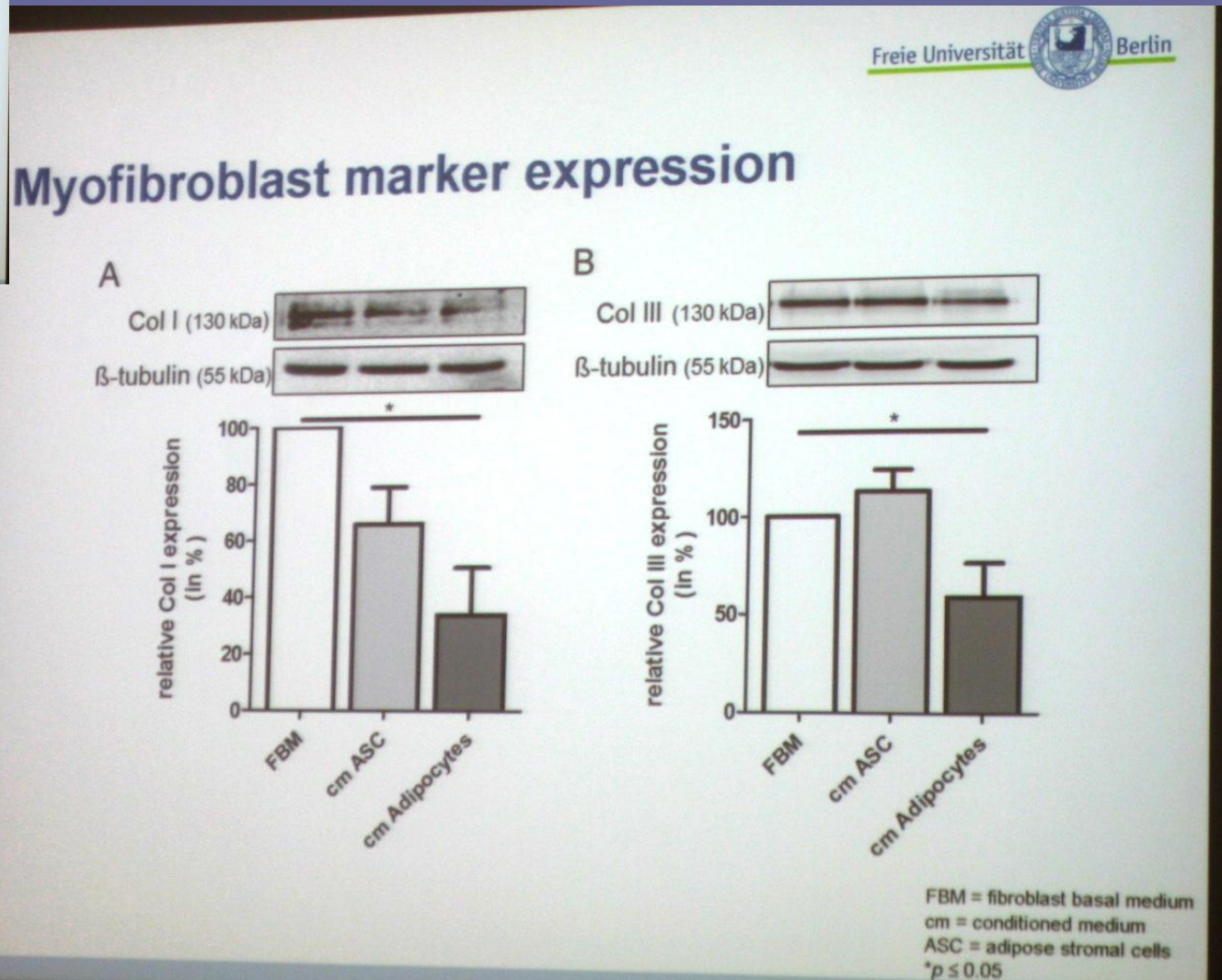
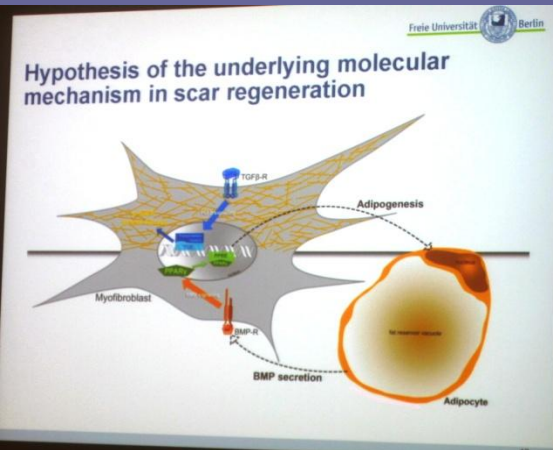
- Сила мышечного сокращения



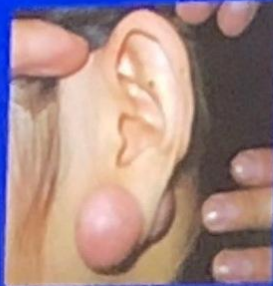
- Количество фибрилл



# Гипотеза о молекулярном механизме ингибирования миофибробластов адипоцитами



## Varieties of keloids



**Should different approaches be applied?**



# Дальнейшее развитие концепции

## Further evolution of the concept

### *Re-examine the "trigger"*

- **The major "trigger" in keloid wounds promoting relapse of surgically removed keloid**
  - Unknown
  - Growth factors
  - Cytokines
  - Angiogenesis
  - Others?
  - **Tension?**

Лечение:  
хирургия  
радиотерапия  
цитостатики  
стероиды  
препараты силикона  
компрессия

## Surgical procedure

- Necessary for large sized keloid
- Necessary for cosmetic effect in some area like earlobe
- Given proper relapse control

## Low dose radiotherapy combined with low dose chemotherapy

- Low dose radiotherapy: increased safety while decreased efficacy
  - How to achieve both efficacy and safety?
  - Combination of radiotherapy and chemotherapy
    - 5-FU injection during surgical procedure and early stage post-OP
    - Application of low dose radiotherapy within 24 hours post-surgery
- 2.5-3 Gray × 4 fractions**

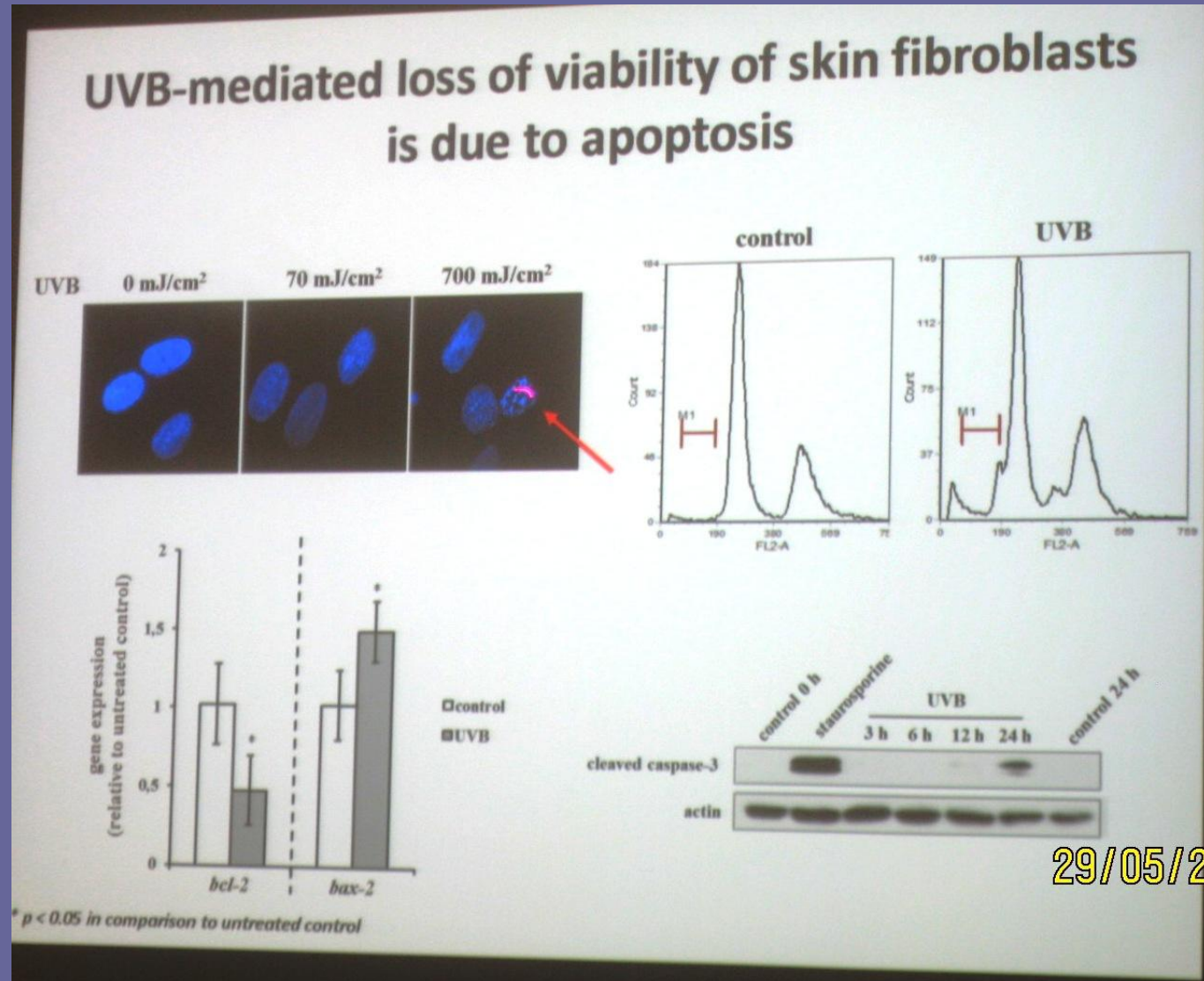
## Concretive therapy

- Drug injection
  - Combined injection of low dose 5-FU and steroid
  - With established protocol for proper control of recurrence
  - Work well for small-sized keloid
  - Difficult for large-sized keloid
- Silicone: suitable for prevention
- Pressure difficult to work alone
- Isotype irradiation less used



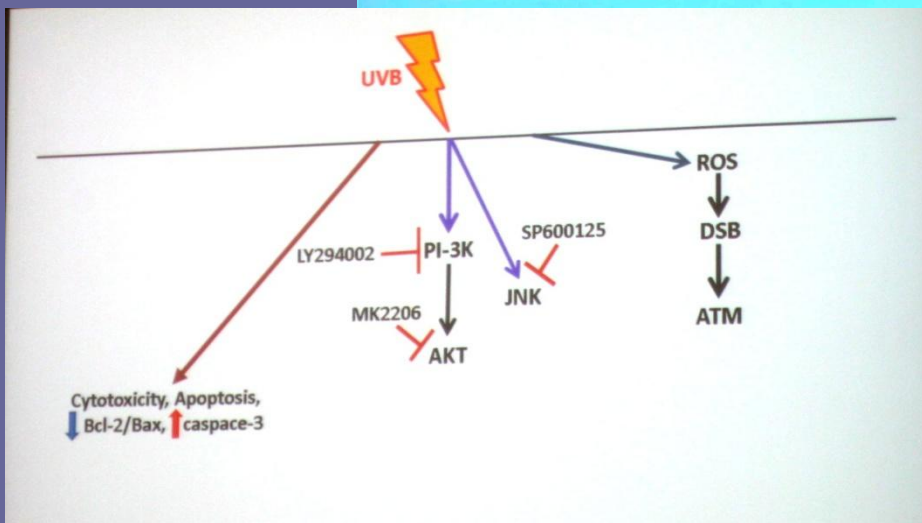
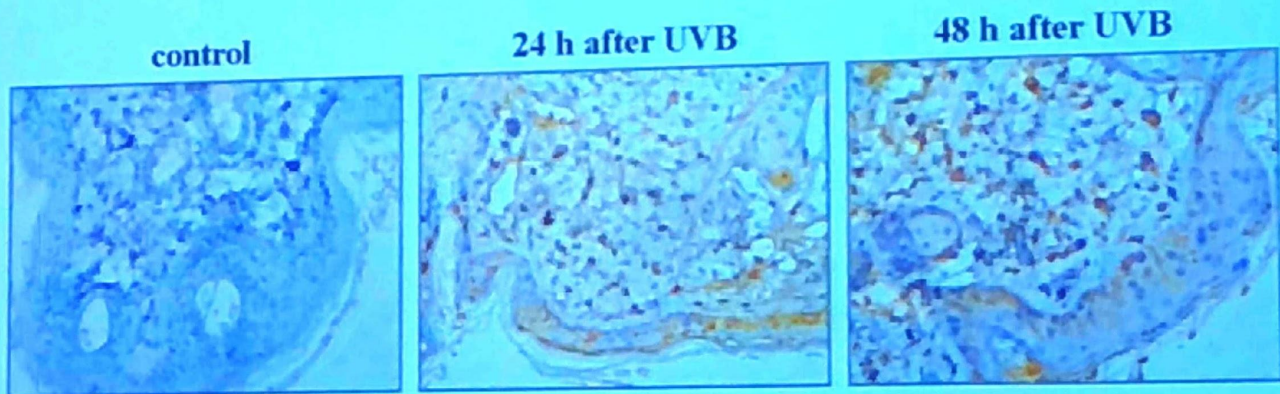
# Влияние УФ облучения

- УФ-опосредованная утрата жизнеспособности фибробластов вследствие апоптоза



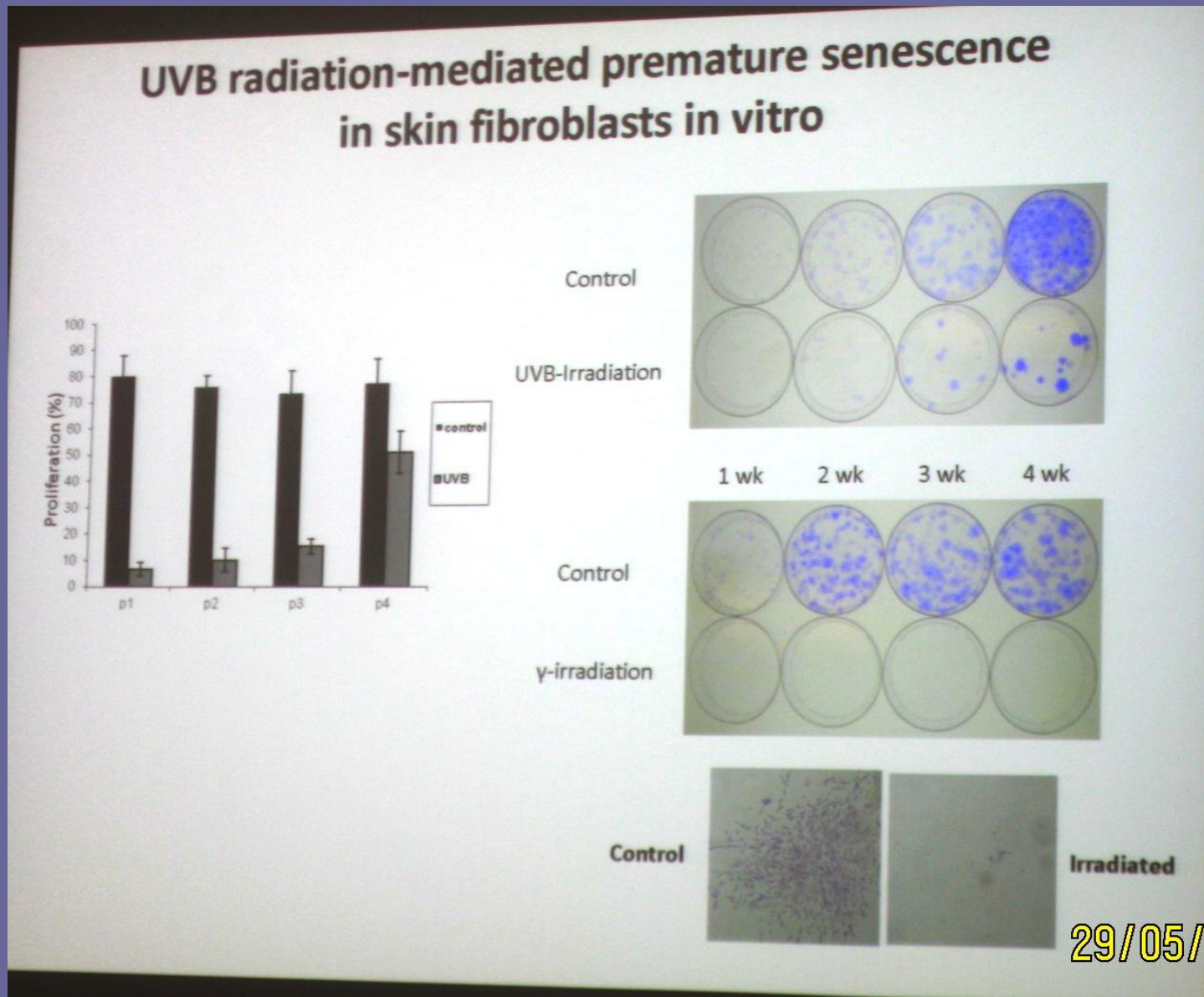
# Каспаза-3 (центральный компонент в механизме апоптоза клетки) активируется в коже мышей после УФ облучения

## Caspase-3 is activated in the skin of SKH1 mice after exposure to UVB radiation





# УФ облучение обуславливает преждевременное физиологическое старение фибробластов кожи



29/05/

# УФ- опосредованное повреждение ДНК активирует онкогены в фибробластах кожи и человека

## UVB-mediated DNA damage activates JNKs and Akt in human skin fibroblasts



29/05/2018



Симптомы зуда имеются у 90% послеожоговых пациентов и у 40% из них он сохраняется до 7 лет после травмы, нарушая сон, повседневную жизнедеятельность и снижая качество жизни.

## Itchy skin / pruritus

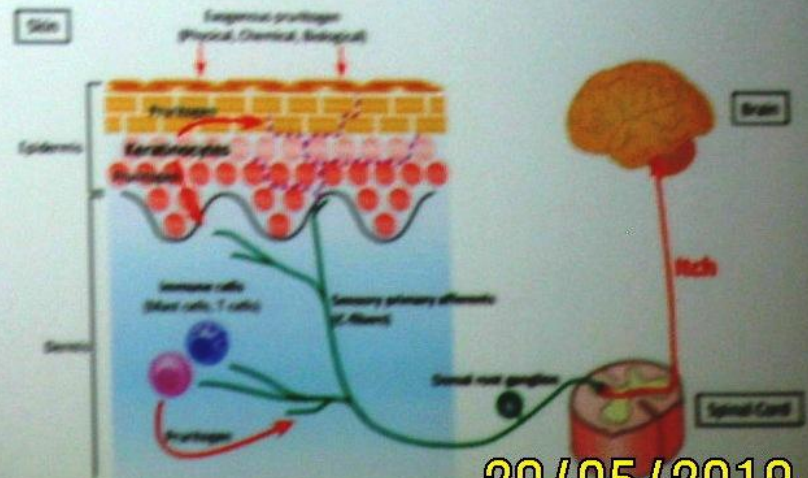


- ▶ Quite common in (deep) scars
  - ▶ Eg. more than 90% of burn patients experience pruritus initially.
  - ▶ A large number of patients with (extensive) scars suffers from long-term itching
    - One study: 40% of burn patients still suffered from itching 7 years after their burn.
- ▶ Very troubling issue that interferes with
  - ▶ sleep,
  - ▶ activities of daily living,
  - ▶ and overall quality of life.

Полного понимания патогенеза зуда в рубцах по-прежнему нет  
Гистамин является одним из самых основных факторов, связанных с  
ощущением зуда

## Itchy skin / pruritus

- ▶ Complete understanding of scar itching is still lacking
- ▶ Many signals and pathways are involved in pruritus
- ▶ Histamine is one of the main factors involved in the sensation of itching
  - ▶ is released by mast cells due to
    - activity,
    - heat,
    - manipulation of the scar,
    - cytokines...
  - ▶ histamine activates histamine receptors
  - ▶ stimulus is then transmitted from particular nerve endings (C fibers) to the brain via specific pathways in the spinal cord.



29/05/2018



# Зуд и сухость рубца

- Системная терапия: антигистаминные препараты и нейропатические препараты

## Treatment of itchy skin

### ▶ Systemic treatment

#### ▶ Oral antihistamines are the first-line treatment for itching.

- first generation anti-histamines (H1-blockers) are the most efficient
- dimetindeenmaleate (Fenistil)
- diphenhydramine (Benadryl),
- hydroxyzine (Atarax, Vistaril),

#### ▶ Neuropathic pain medication

- Cfr. similar pathways involved in itch and pain
- gabapentin (Neurontin) (anti-epilepticum and treatment of nerve-related pain (eg. in diabetes)
- naltrexone (Narcan) (which acts on opioid receptors involved with pain perception)
- amitryptiline (Redomex) and other antidepressants.

# Лечение сухости кожи актуальные продукты для уменьшения зуда

## Treatment of itchy skin

- ▶ Treatment of dry skin
  - ▶ Reduction of frequency of bathing
  - ▶ Cleansing of the skin with moisturizing washing products
  - ▶ Hydration of the skin with hydrating topicals in sufficient amounts
- ▶ Specific topical products to reduce itch
  - ▶ Cooling agents, such as menthol or camphor
  - ▶ Colloidal oatmeal, used in moisturizers or bath products
  - ▶ Topical silicone gel
  - ▶ Capsaicin



# Влияние макрофагальной реакции на адаптацию имплантатов

## Major problems in implantation



- Adverse reactions of immune cells to the material itself
- Formation of bacterial biofilms on implant surface which is followed by chronic inflammation and implant loosening
- Wearing of the implants as a result of prolonged mechanical pressure that leads to the release of wear particles

# Использование программирования макрофагов при помощи цитокинов в терапевтических целях

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## Macrophages as diagnostic biomarkers and cell therapy tools

Diagnostics: diseases, response to treatment in personalised medicine

Monocyte → Macrophage

**Therapy**

Targeting of macrophages:

- Elimination
- Inhibition of recruitment
- Reprogramming in vivo

**Macrophages as cell therapy to**

- Programming ex vivo
- Delivery

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## Implants and biomedical devices

**Implants and biomedical devices** are used in different fields of medicine to support, enhance or replace an existing biological structure

Adjustable Gastric Banding

31/05/2018

Image source: Wikimedia Commons

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## IMMODGEL concept

Local immunomodulation around implants by innovative auxiliary hydrogel-based systems encapsulating autologous and phenotype controlled macrophages

**Titanium Implants**

**Conventional** → **Implantation**

CHRONIC INFLAMMATION, REJECTION

Predominantly M1 macrophages in the microenvironment

**IMMODGEL**

Encapsulated M2 macrophages Adhered to the Implant

HEALING, INTEGRATION

Increase of M2 macrophages in the implant microenvironment

31/05/2018

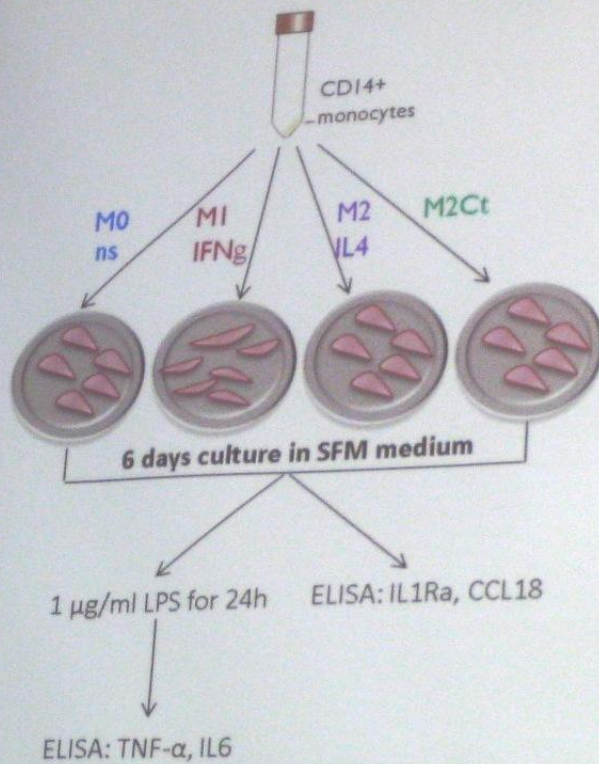


# Модификации макрофагов

UNIVERSITÄT  
HEIDELBERG



## Stimulatory cocktail M2Ct: Suppression of inflammation



M1 cytokines: TNF- $\alpha$  and IL6 are mediators of acute phase of inflammation. They are induced by macrophage contact with biomaterials

M2 cytokines: IL-1Ra is an anti-inflammatory cytokine that favors wound healing;  
CCL18 is a sensitive marker of M2 polarization

**IFNg:** 100 ng/ml

**IL4:** 10 ng/ml

**M2Ct:** IL4 (3 ng/ml)+IL10 (10 ng/ml)+TGF $\beta$ 1 (10 ng/ml)

SFM + M-CSF (10 ng/ml) + Dexamethasone ( $10^{-8}$ M)

IF- $\alpha$  and IL6 are detectable only after LPS challenge

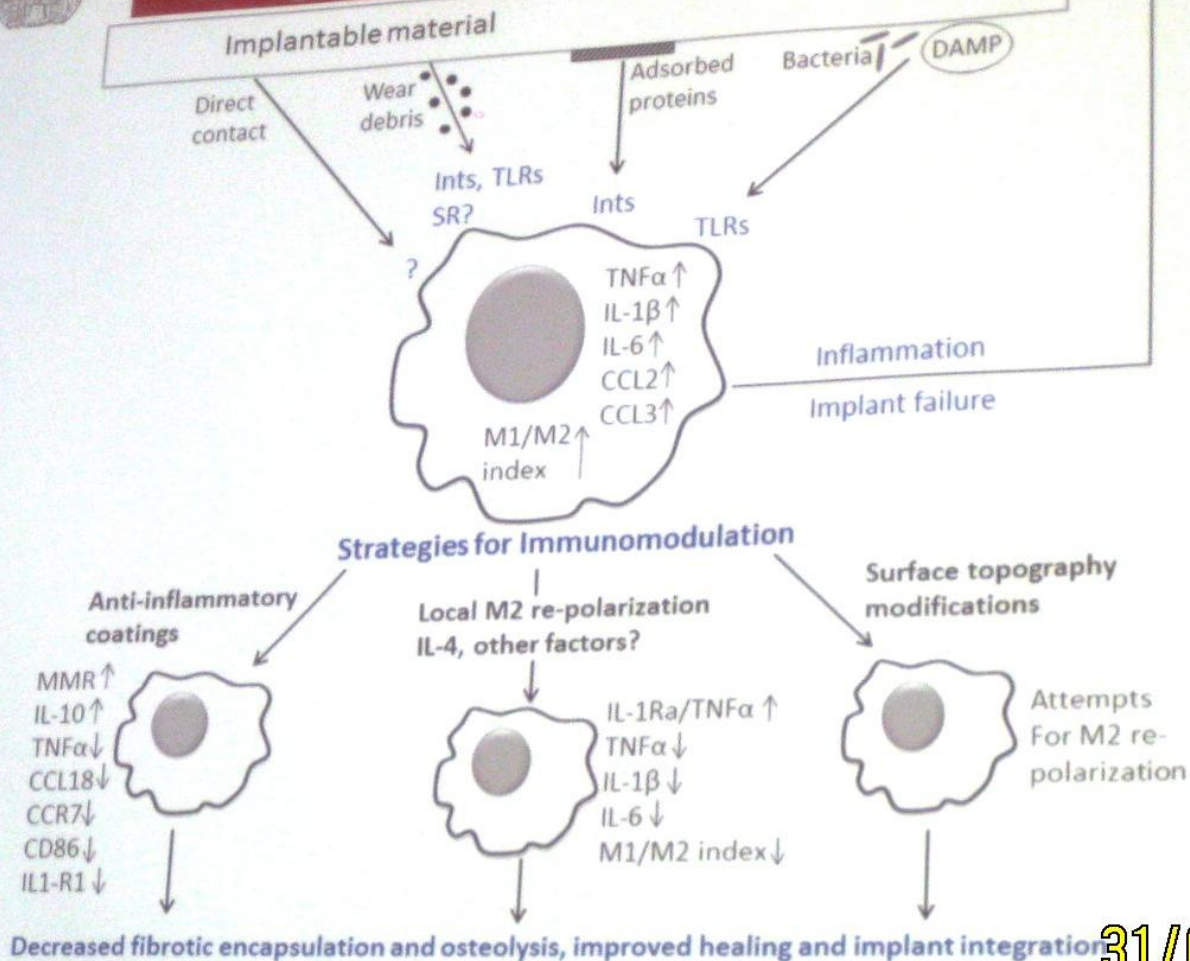
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# Стратегия иммуномодуляции



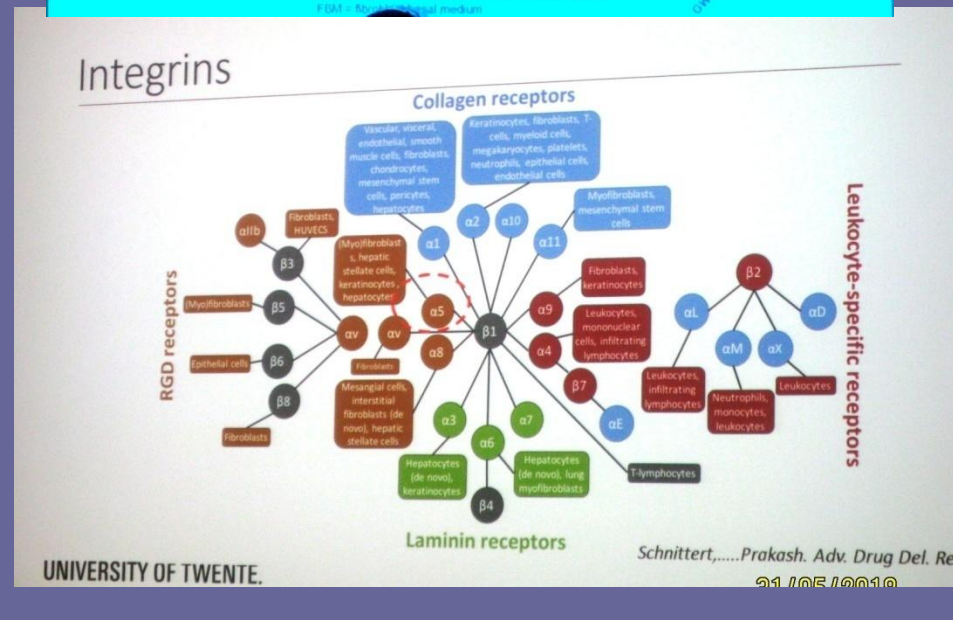
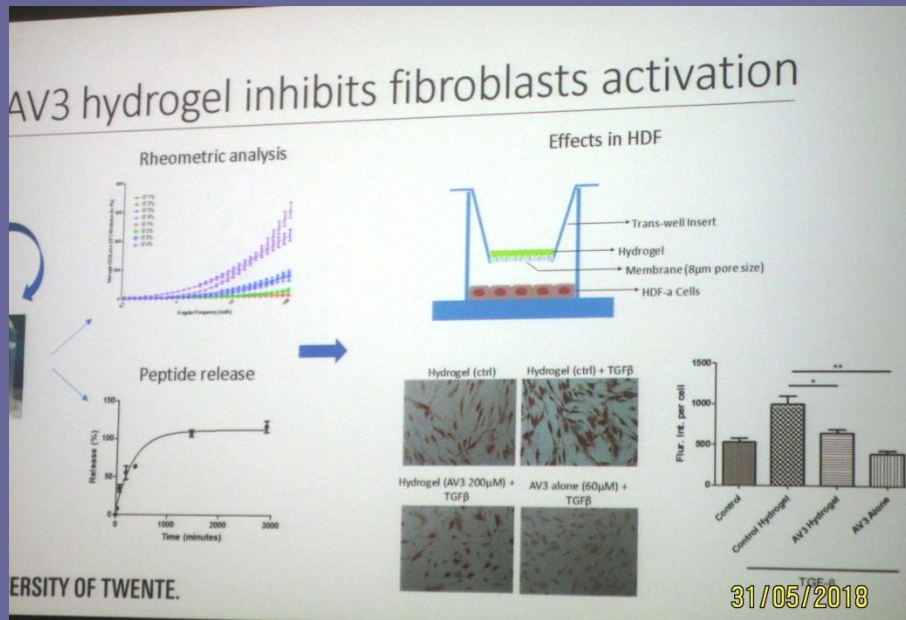
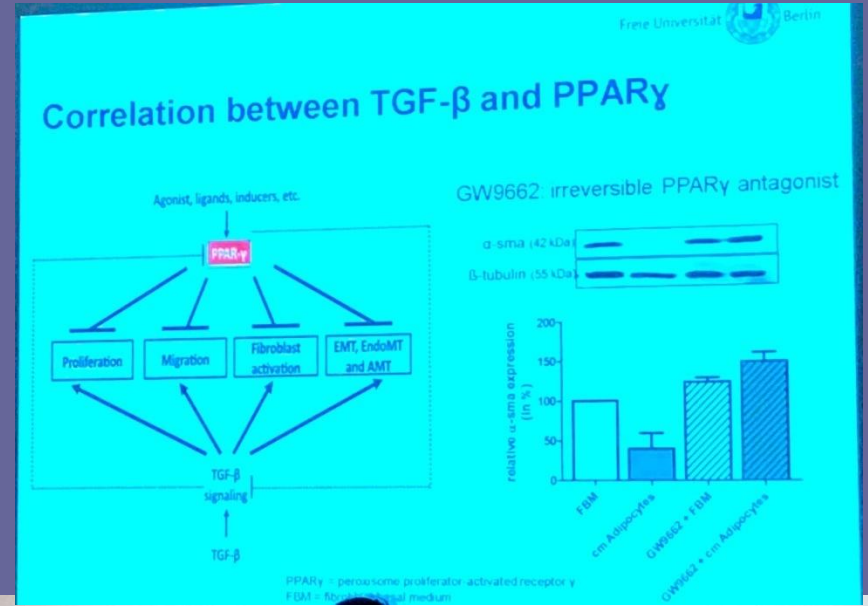
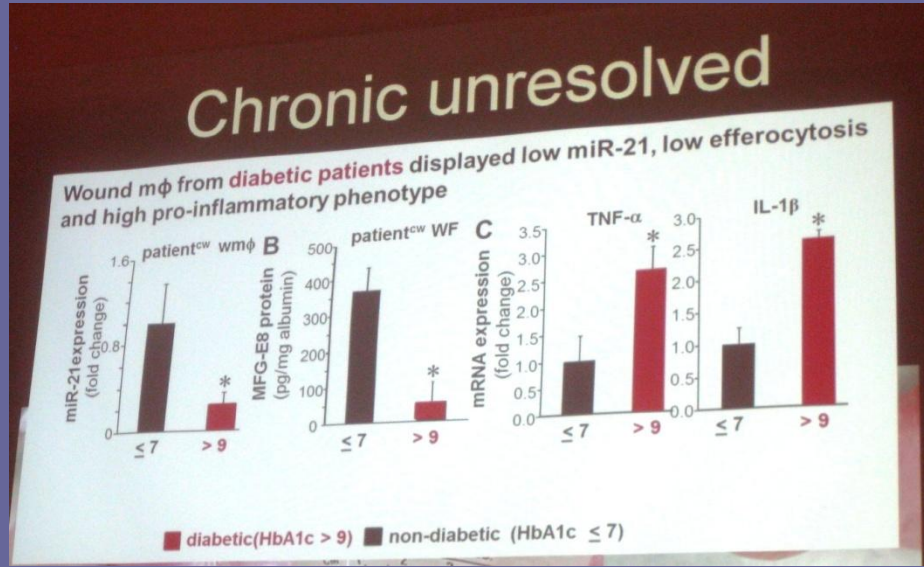
## Macrophages mediate foreign body response to implant



31/05/2018



# Изучаются сигнальные пути взаимодействия ферментов, генов, цитокинов и рецепторов



# Выставка

+ 31 (0)55 355 2580 info@scarban.eu 09:00-17:30

## Scarban®

### SCARBAN SILICONE SCAR SHEET AND GEL

SCARBAN SILICONE SHEET AND GEL

- Proven, effective scar treatment
- Also reduces itching and pain
- Most recommended by professionals



**Scarban Elastic Silicone Sheet**

- Intensive therapy – highly effective
- Suitable for small and large areas of skin
- Includes very high-level UV



**Scarban Light Silicone Sheet**

- Thinner and more flexible
- Ideal for sensitive skin
- Includes very high-level UV protection



**Scarban Velvet Touch Silicone Gel**

- Invisible scar therapy
- Quick-dry (wear under makeup!)
- Convenient container with dosage pump





## Helps repair the skin

- Less itch
- Less pain
- Fewer Scars



### Experiences with Alhydran

What others say

Our four-year-old daughter was scalded by hot water. She still had a lot of unpleasant symptoms 1½ years later. ALHYDRAN made our daughter's skin more supple. Now her skin is much less itchy and red. And her scar has improved visibly too!



Impressive skin improvement

[Read more experiences with ALHYDRAN](#)



Order ALHYDRAN? Contact us

Helps your skin recover

Effective and proven

## SILVERLON®

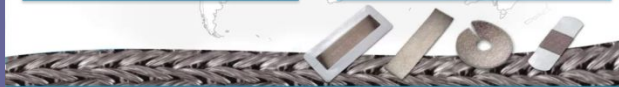
safe, strong, simple™

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International

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### BENEFITS

TheraBond® 3D with unique SilverTrak™ technology provides the powerful combination of antimicrobial protection, adaptive fluid transport, and flexible strength

- Rapid, controlled, and sustained release of ionic silver in the dressing kills pathogens for up to 7 days<sup>1</sup>
- Unique capillary-like action transfers excess fluid and exudate into an absorbent outer dressing
- Flexible strength of the fabric moves with the patient to minimize friction; durable design supports extended wear



Up to 7 days of proven broad-spectrum antimicrobial protection against pathogens

- **Immediate action:** Kills pathogens on contact<sup>1</sup>
- **Rapid onset:** Achieves a 99.99% reduction (4 log10) in colony-forming units of a broad range of pathogens<sup>1</sup>
- **Sustained release in the dressing:** Effective barrier to pathogens for up to 7 days<sup>1</sup>

PATHOGEN REDUCTION LOG <sub>10</sub> (X)		7-DAY BARRIER STUDY		Inoculum Concentration (CFU/mL)
Test Organism	24 Hours	Test Organism	Results	
S. aureus	>5.11	S. aureus	no growth	2.44 x 10 <sup>6</sup>
MRSA	>5.22	MRSA	no growth	2.19 x 10 <sup>6</sup>
VRE	>5.43	VRE	no growth	1.51 x 10 <sup>6</sup>
P. aeruginosa	>5.03	P. aeruginosa	no growth	1.01 x 10 <sup>6</sup>
E. coli	4.82	E. coli	no growth	1.04 x 10 <sup>6</sup>
Aspergillus brasiliensis	4.80	Aspergillus brasiliensis	no growth	2.55 x 10 <sup>6</sup>
Candida albicans	>5.11	Candida albicans	no growth	2.40 x 10 <sup>6</sup>

### Featured Products

- Surgical Site Dressings
- Burn Care Dressings
- Wound Care Dressings

### Request Clinical Evaluation

See how TheraBond antimicrobial dressings perform in your healthcare organization

[Request Clinical Evaluation](#)

### Scientific Research

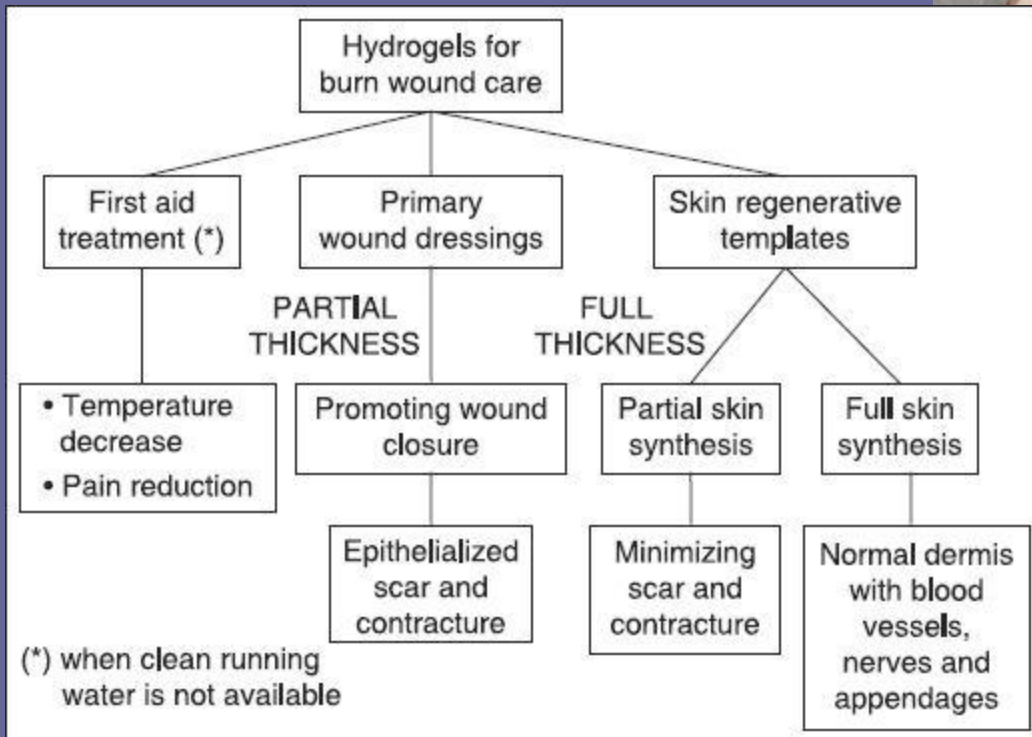
Please note that these studies may involve findings that exceed the claims currently cleared by the FDA for the product. Argentum Medical, LLC is not intending to make performance claims about its product. The intent is to disseminate the scientific literature on these products. We encourage you to read these studies to understand the strengths and limitations of the data. For some claims, Argentum is seeking to broaden the indications with the FDA in the future using data, such as these studies, to provide the substantiation.

- Huckfeldt et al: [Early Bactericidal Activity of Sputtered Nanocrystalline Silver versus Electroless Autocatalytically Plated Silver](#)
- Huckfeldt et al: [Three Dimensional Silver Fabric Technologies Provide an Advanced Antimicrobial Wound Management System](#)
- Huckfeldt et al: [The Efficacy of Five Silver Based Dressings on Concentrated Acinetobacter](#)

# Гидрогелевая маска:

- обезболивание
- барьер для микроорганизмов и потери влаги
- комфорт для пациента
- оптимальная среда для эпителизации

**BurnTec**<sup>®</sup>  
FIRST AID FOR BURNS





# Достопримечательности



28/05/2018



## Заансе Сханс - деревня мельниц

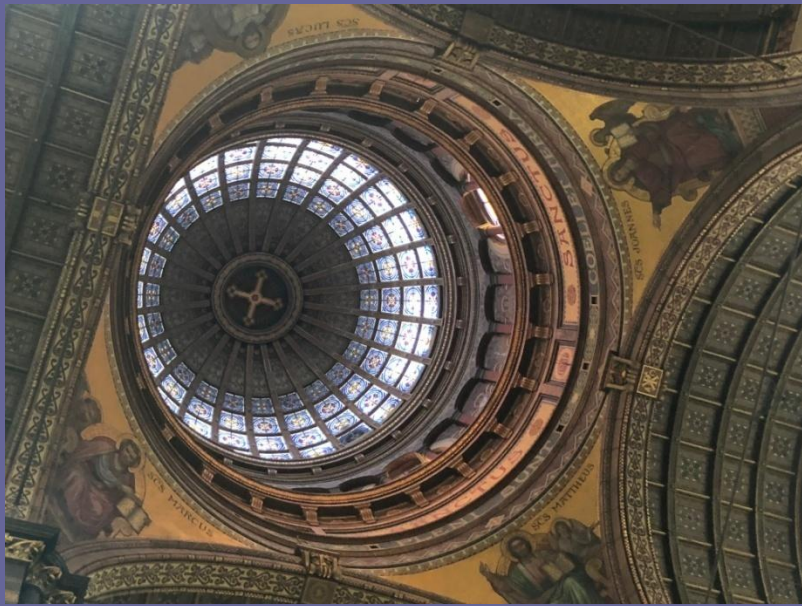






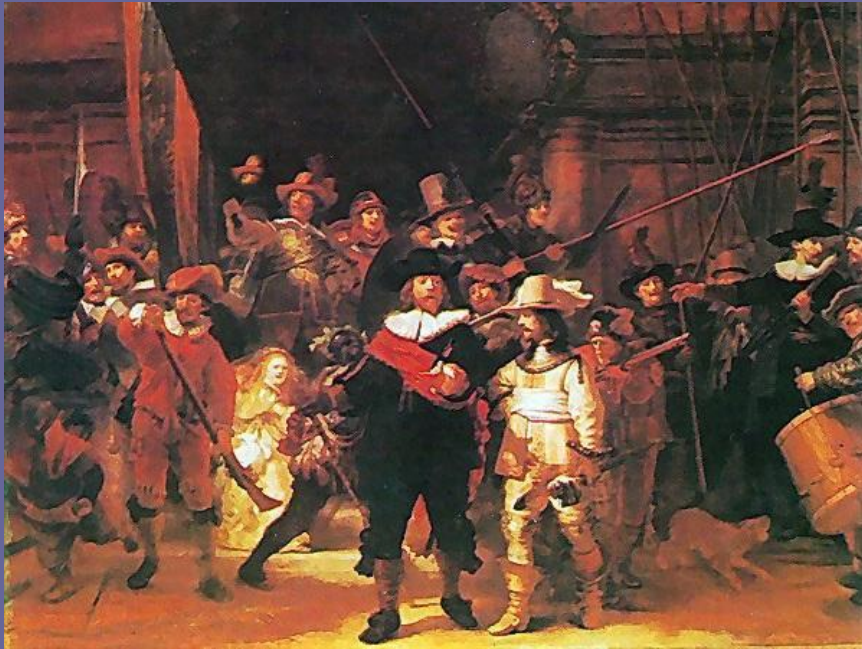


# Церковь святого Николая





# Памятник Рембрандту





# Цветочный рынок





# Цветочный рынок









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ВНИМАНИЕ!**

**I amsterdam**

