



**PLATELET RICH PLASMA
APPLICATIONS on BURNS; ULCUS;
DIABETICS and CHRONICS WOUNDS**

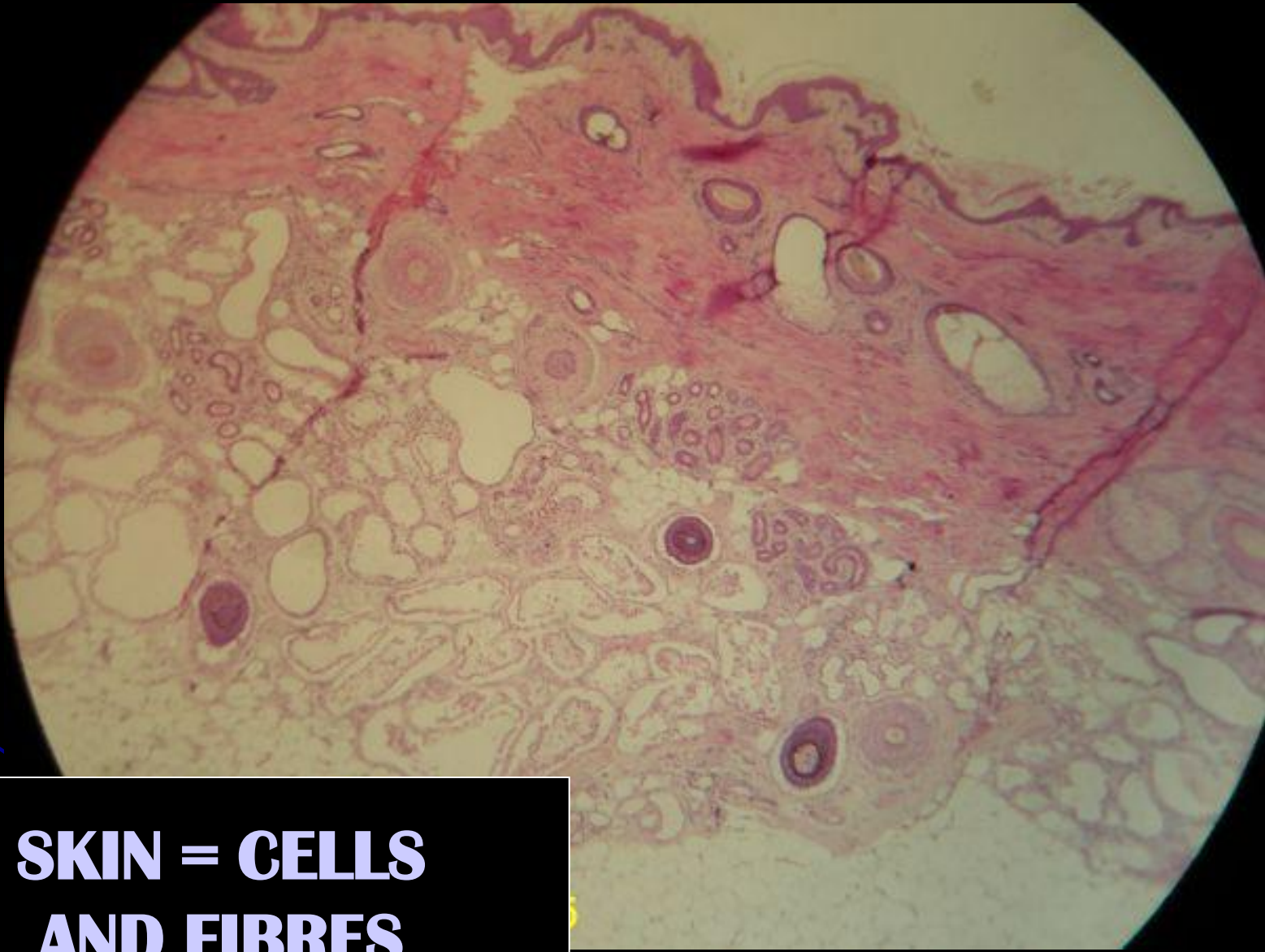
**PHLEBOLOGY FRENCH. SOC. ANNUAL CONGRESS
PARIS January 2014 the 31 ST**

**Dr Bruno Bioulac
Department for Plast Chir
HOSPITAL OF FREUDENSTADT
GERMANY
Secretary 0049 7441 54 64 11**



SKIN

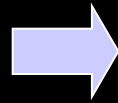
HISTOLOGIE-BIOLOGIE



**SKIN = CELLS
AND FIBRES**

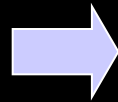
SKIN

- EPIDERMIS



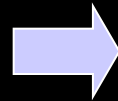
- KERATINOCYT

- DERMIS



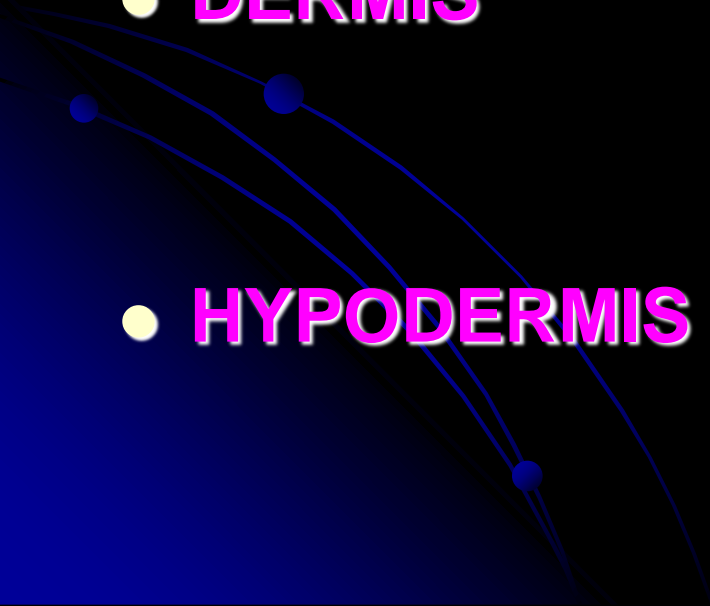
- FIBROBLAST

- HYPODERMIS

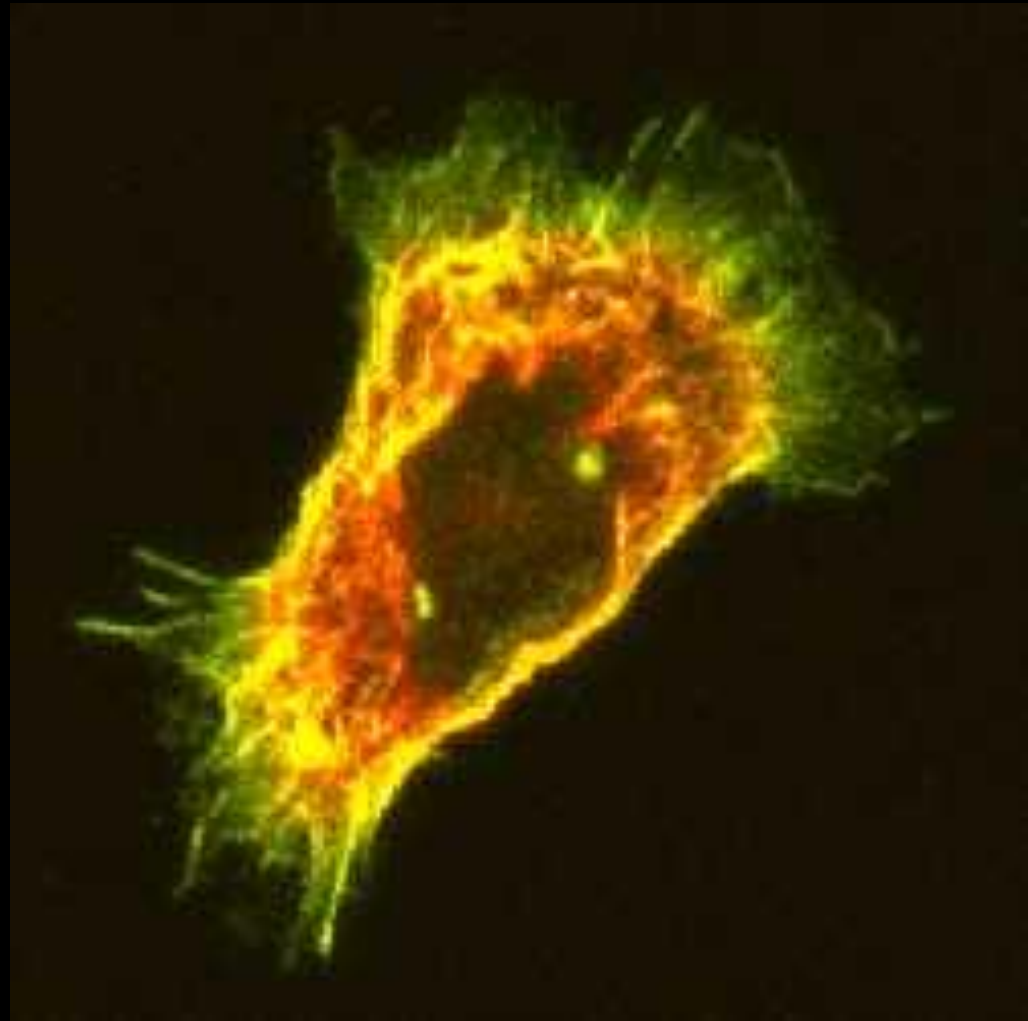
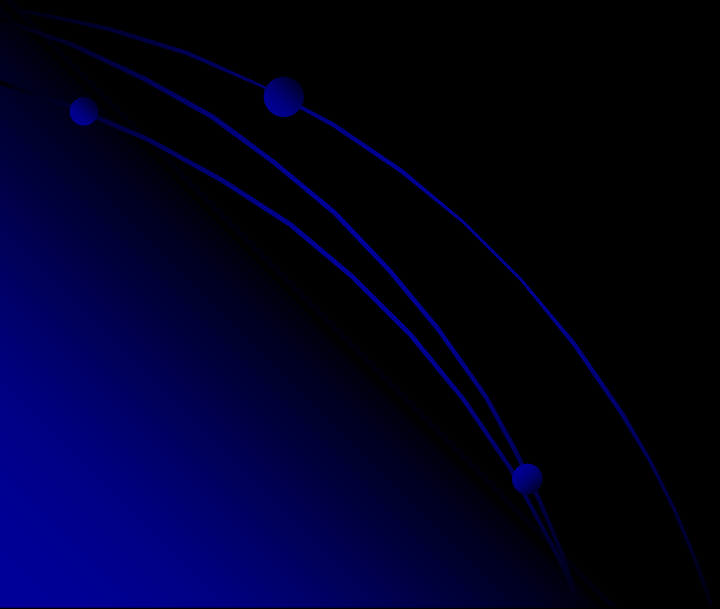


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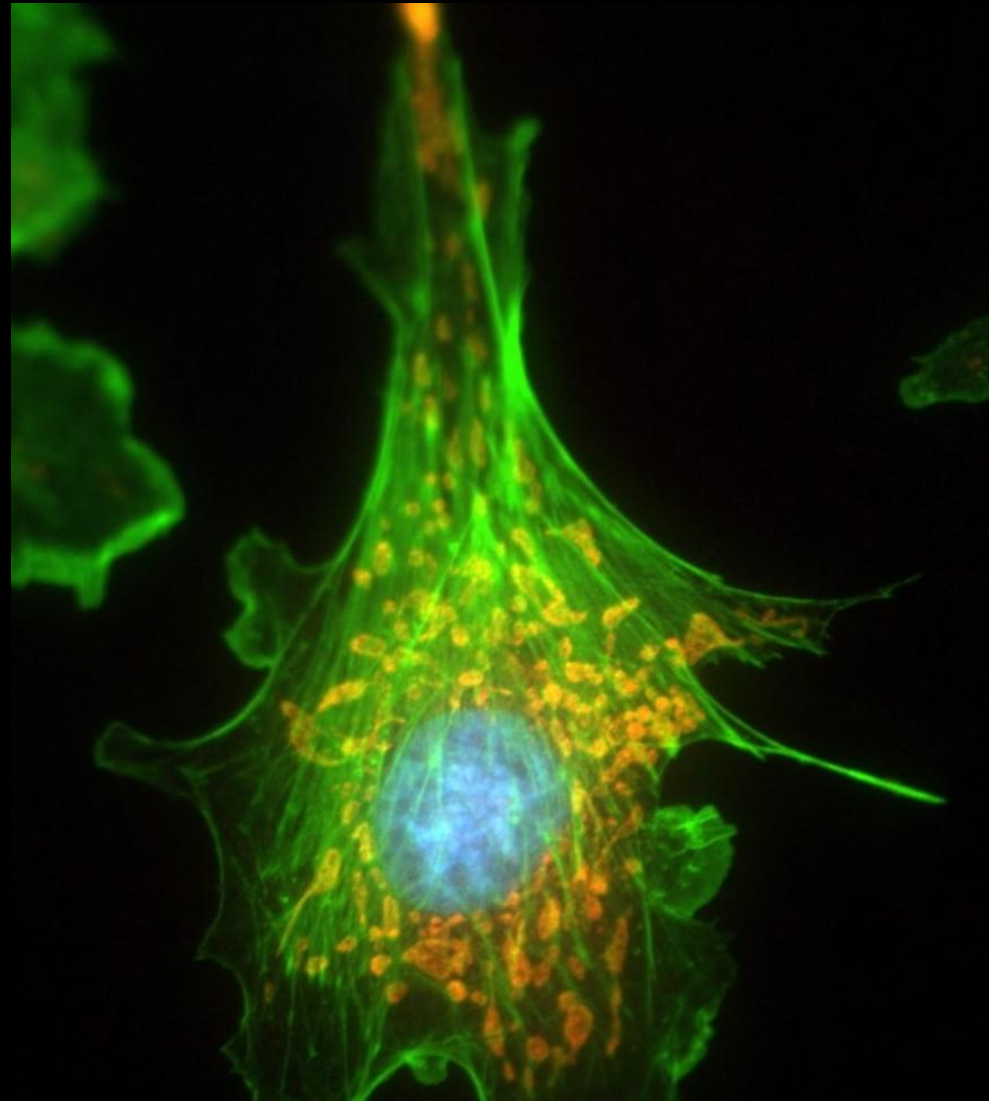
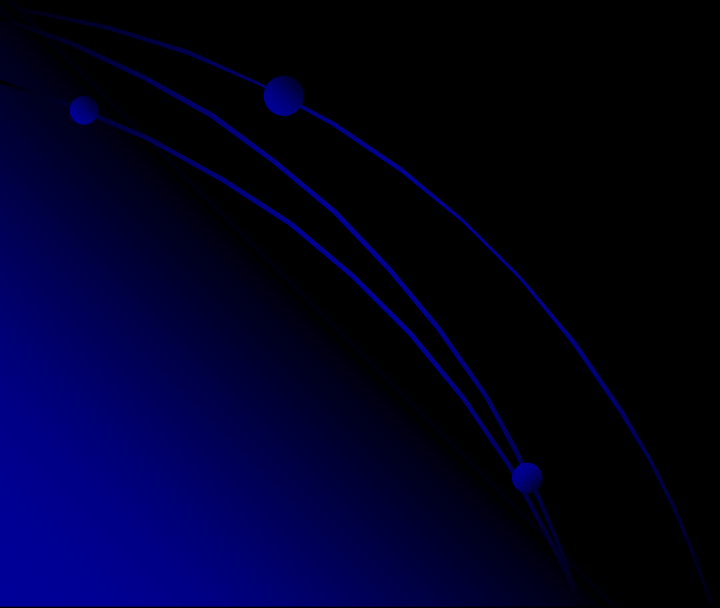
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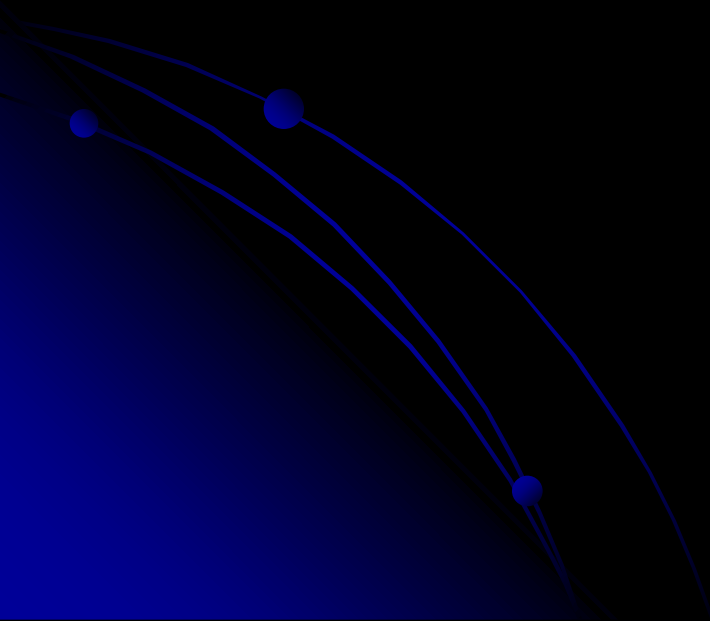
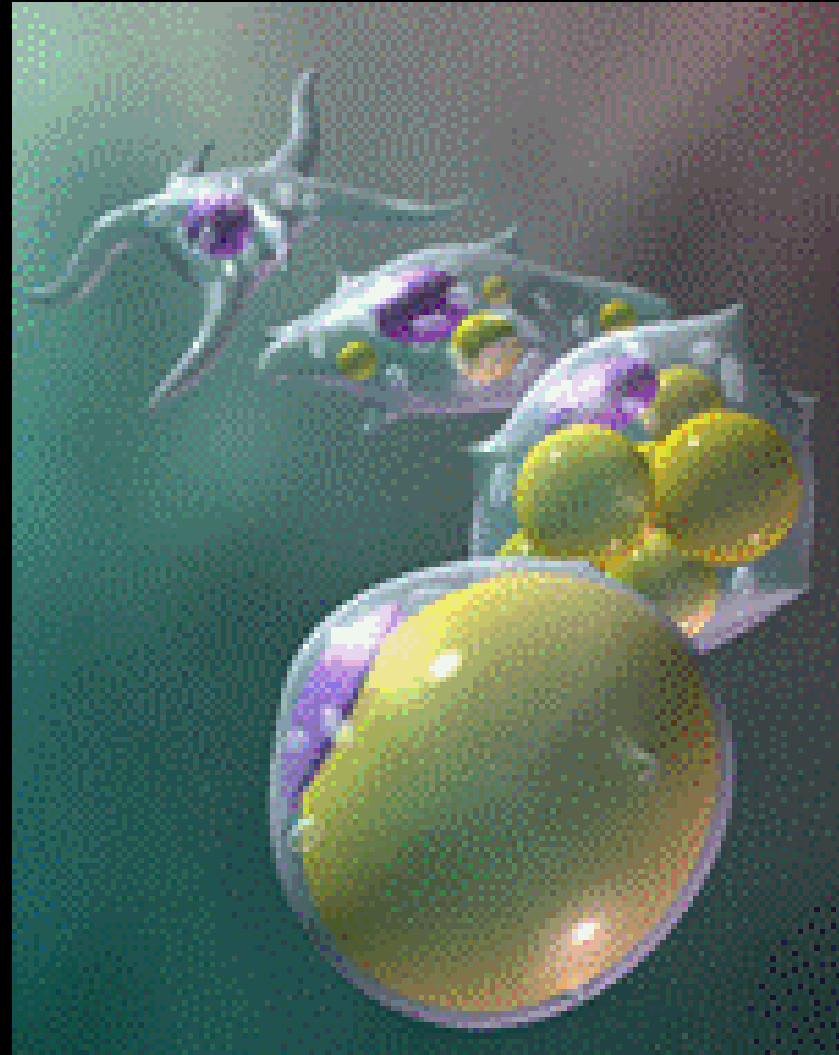
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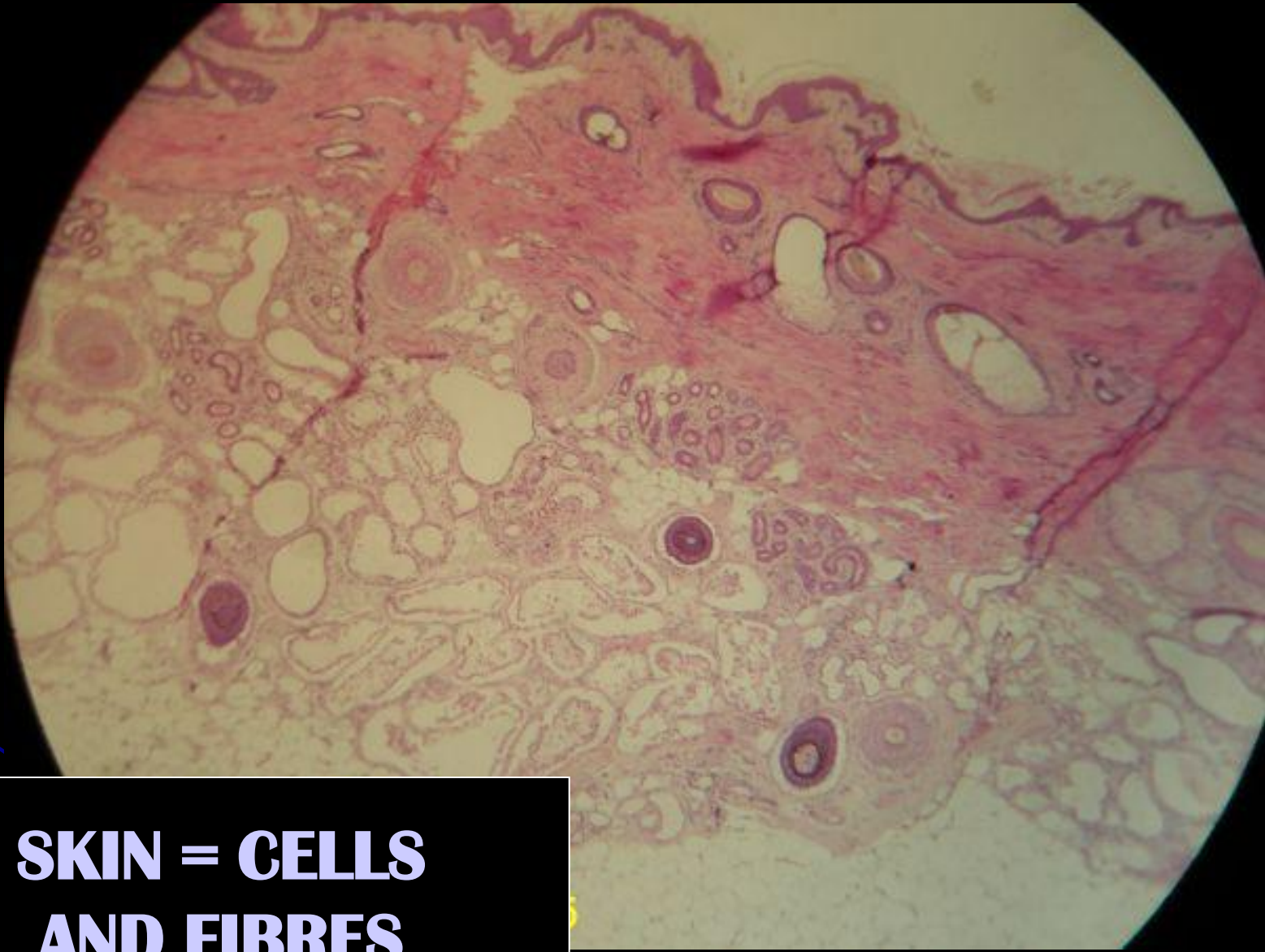


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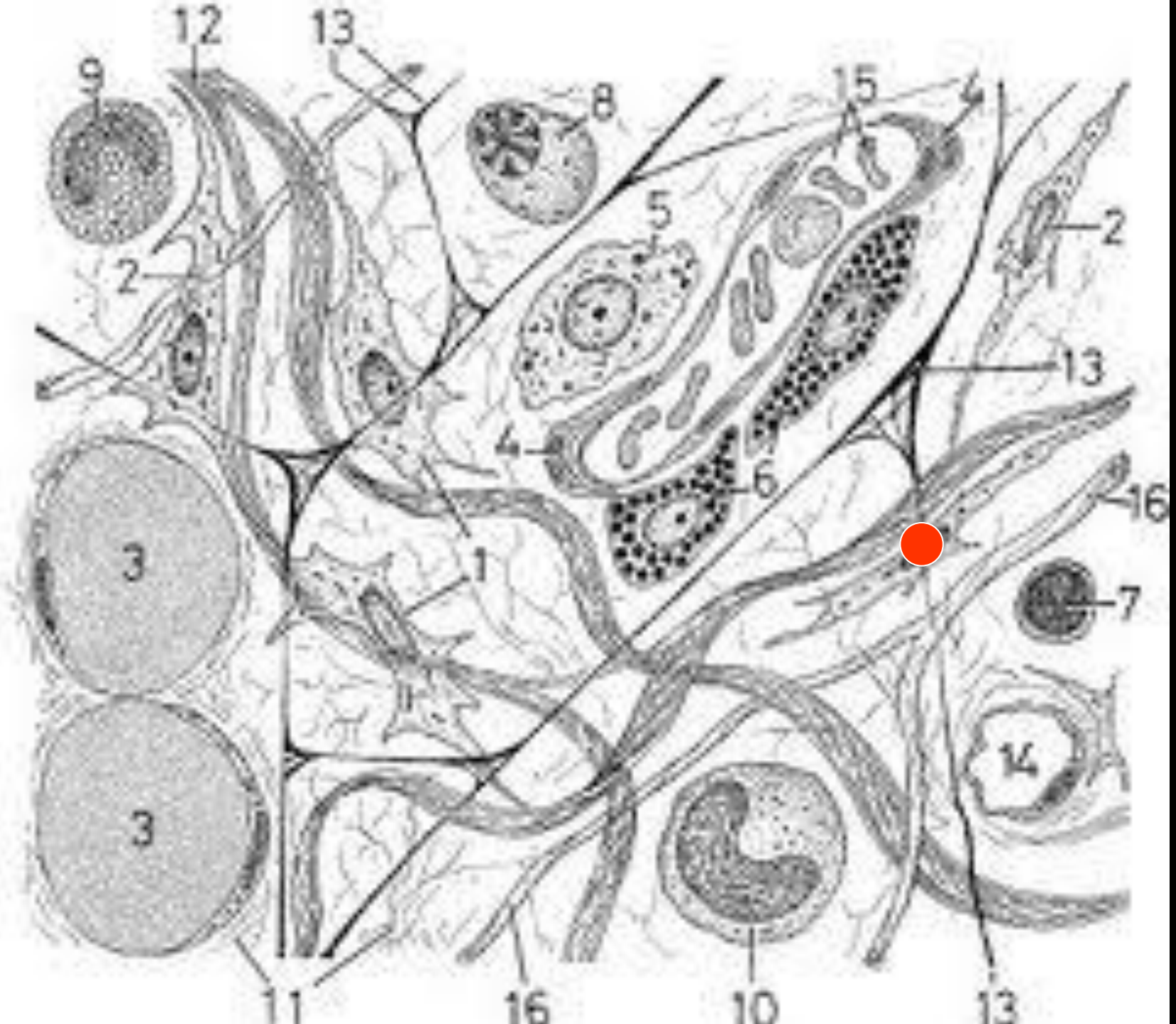


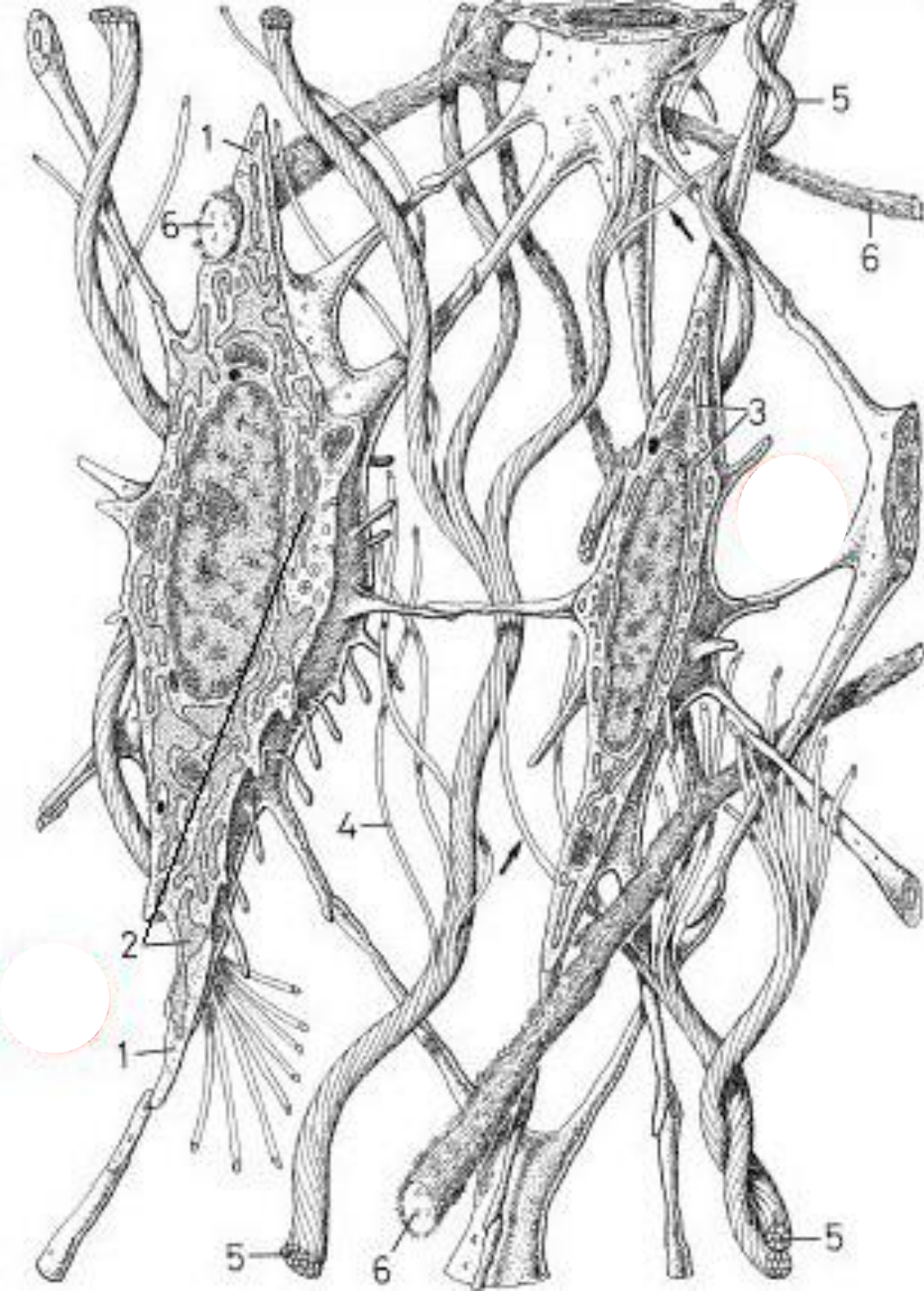
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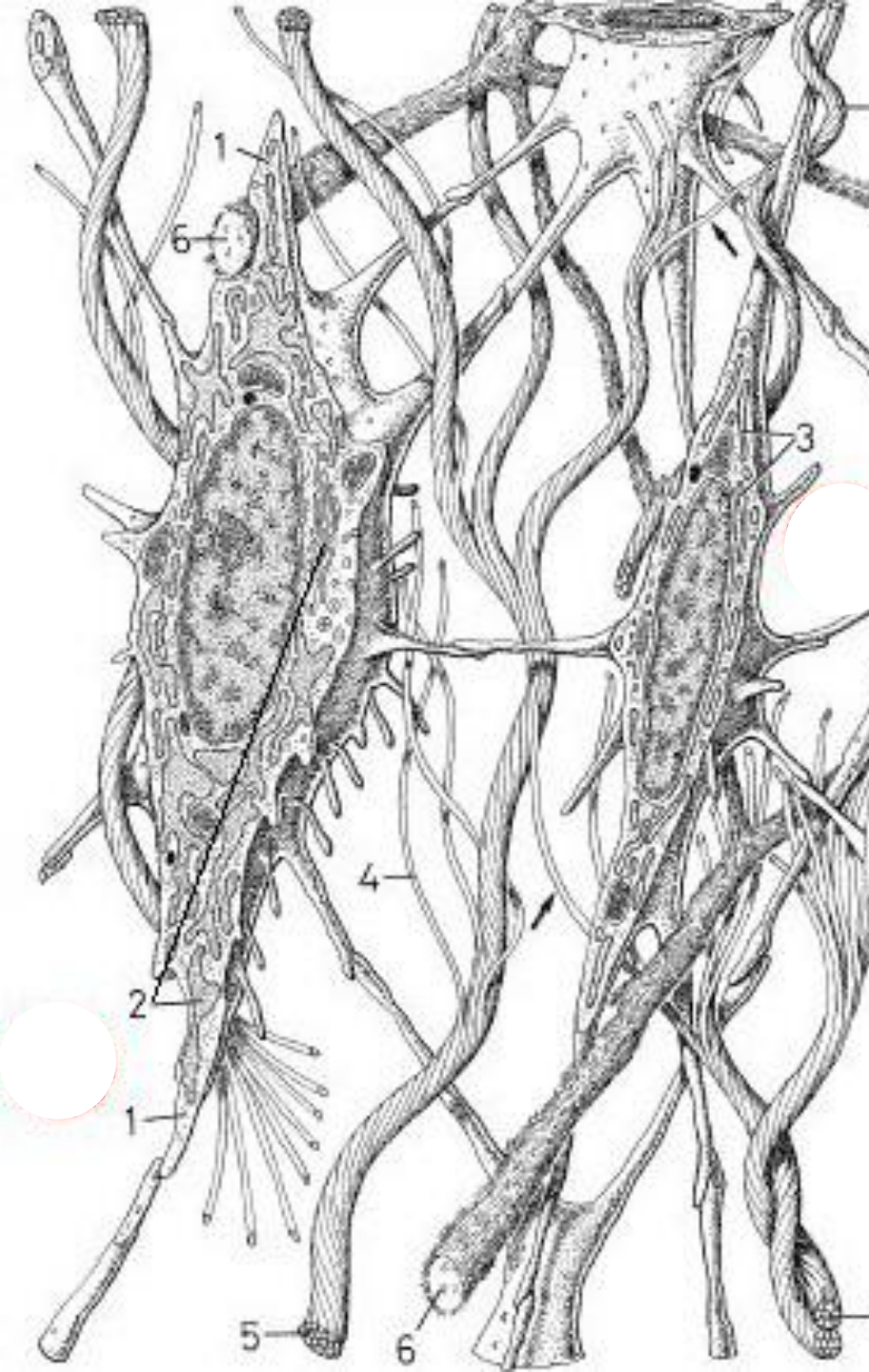




**SKIN = CELLS
AND FIBRES**





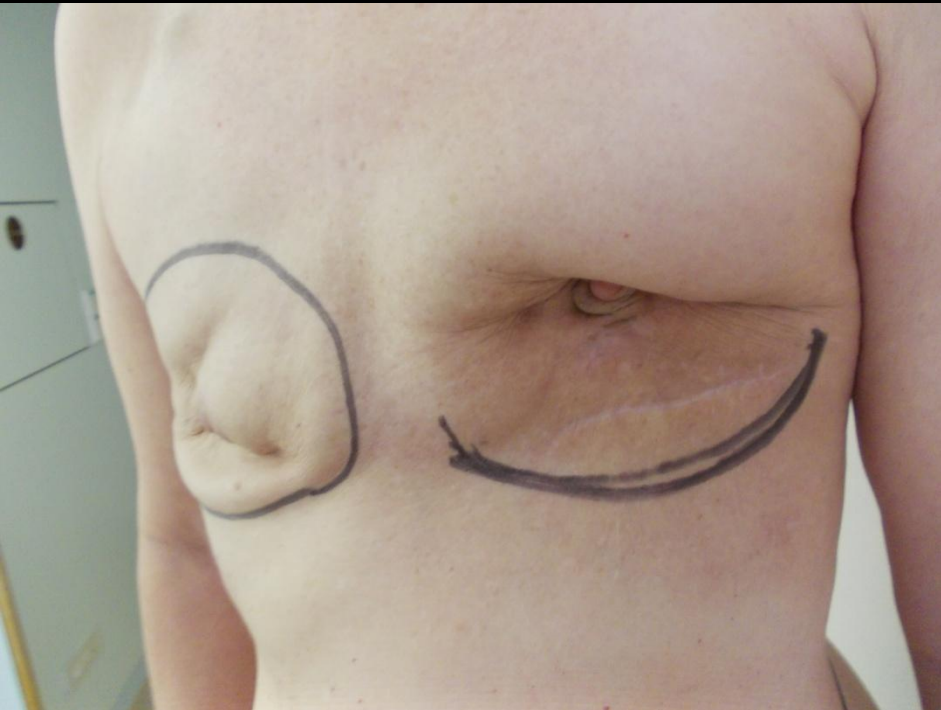


**65 % of a body is
CONJONCTIV TISSUE
100 % ARE FIBROBLASTS**











P.R.P.
PLATELET RICH PLASMA

PRP

Plasma + Platelet * 2

Blood Cells

25/2/2011 17:30



Platelet

Albumine. : + de 50 %

Anticorps (= Immunoglobulines):
20 % (essentiellement des IgG)

Fibrinogène : 5 %

Alpha 1 antitrypsine : 4 %

Alpha 2 macroglobuline : 4 %

Transferrine : 3 %

Lipoprotéines (HDL et LDL) : 8 %

25/12/2011 17:30





**P.R.P.
IN HOSPITAL**

GYNECOLOGIE

BREAST CENTER
Plastic Surgery

**PLASTIC ESTHETIC
SURGERY**

Reconstruction

Classic Laps
Skin transfert

**Tissue
Regeneration**

FET TRANSPLANTATION

P.R.P.

**MESENCHYMALES
STEM CELLS**

GYNECOLOGIE

BREAST CENTER
Plastic Surgery

PLASTIC ESTHETIC SURGERY

Reconstruction

Classic Laps
Skin transfert

Tissue Regeneration

FET TRANSPLANTATION

P.R.P.

HEALING PROBLEMS

MESENCHYMALES STEM CELLS



9/9/2008 10:53



COTATION SYSTEM DRG

| | |
|--------------------|--------|
| ● DRG K 60 D | 2900 e |
| 18,3 % ----- | 530,70 |
| ● DRG F 27 C | 2900 e |
| 19,9 % ----- | 577,10 |



HEALING PROCESS

HEALING PROCESS

Phenomene Inflammatoire et Cicatriciel

COAGULATION

INFLAMATION

ANTI
INFLAMATION

REGENERATION

PAIN KILLER

REGENERATION
CYTOKINES
PRO INFLAMAT

REMODELLING
MUSCLE LISSE

P.R.P.

Phenome
Inflamatoire
et Cicatriciel

COAGULATION

INFLAMATOIRE

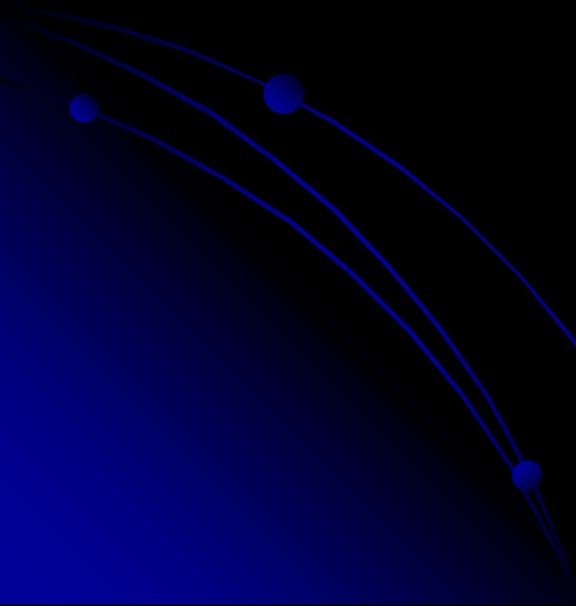
**ANTI
INFLAMATOIRE**

REGENERATION

ANTALGIQUE

**REGENERATION
CYTOKINES
PRO INFLAMAT**

**REMODELLAGE
MUSCLE LISSE**



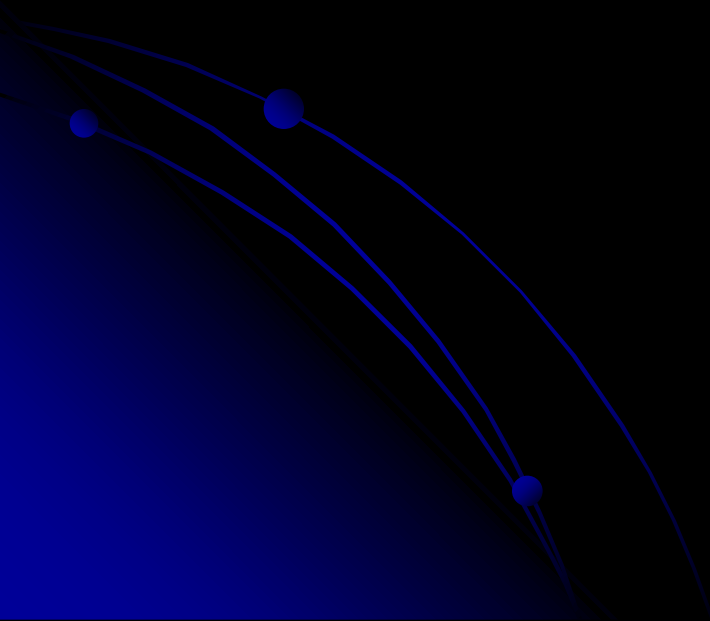
HEALING PROCESS

HEMOSTASIS

INFLAMATION

REGENERATION

REMODELLING



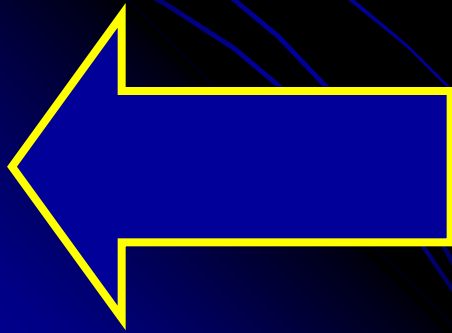
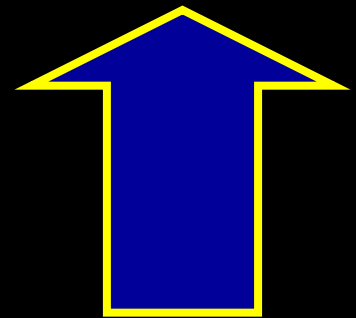
HEALING PROCESS + PRP

HEMOSTASIS

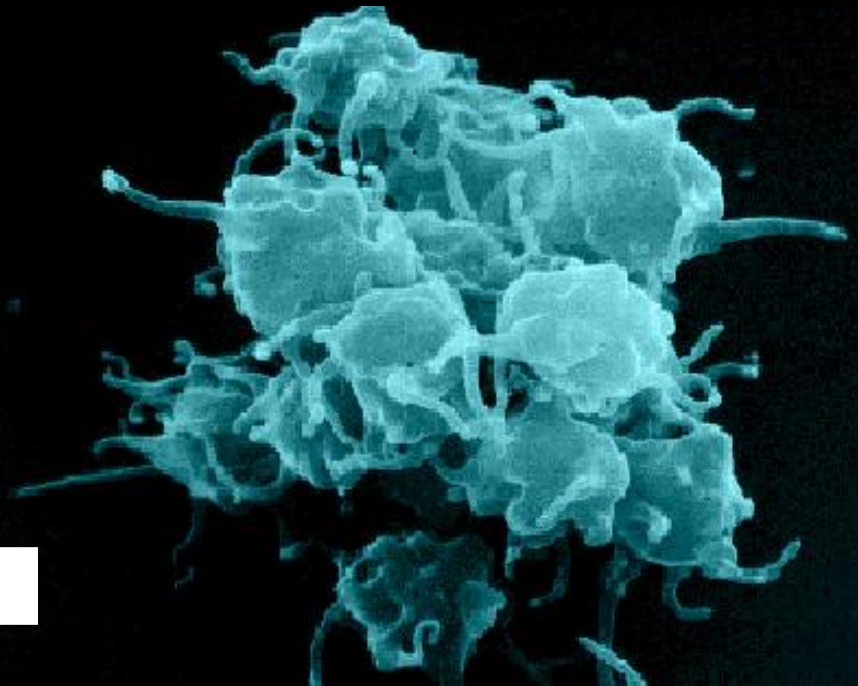
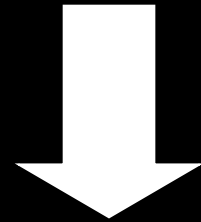
INFLAMMATION

REGENERATION

REMODELLING



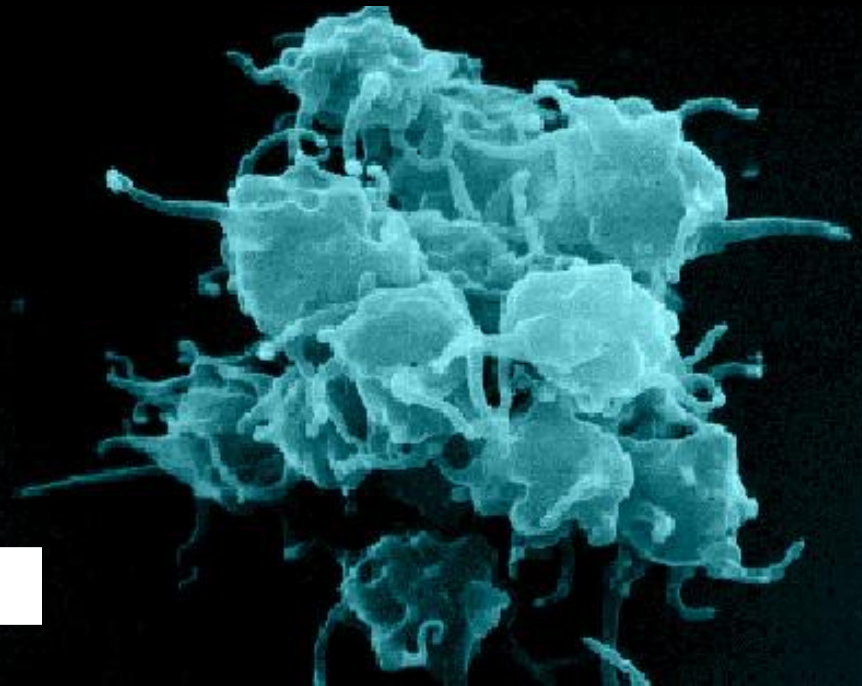
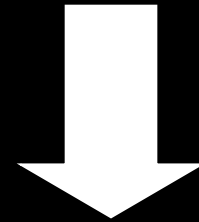
**PLATELET
ACTIVATION**



Coagulation



**PLATELET
ACTIVATION**

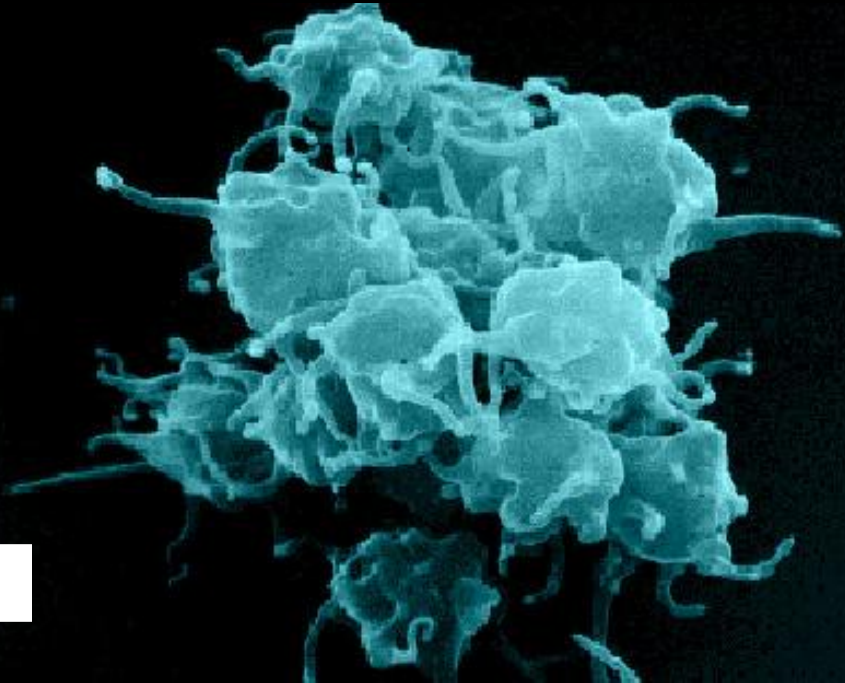
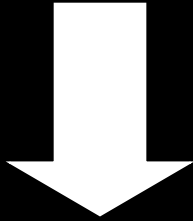


**INFLAMMATION
HEALING PROCESS**





**PLATELET
ACTIVATION**



GROWFACTORS

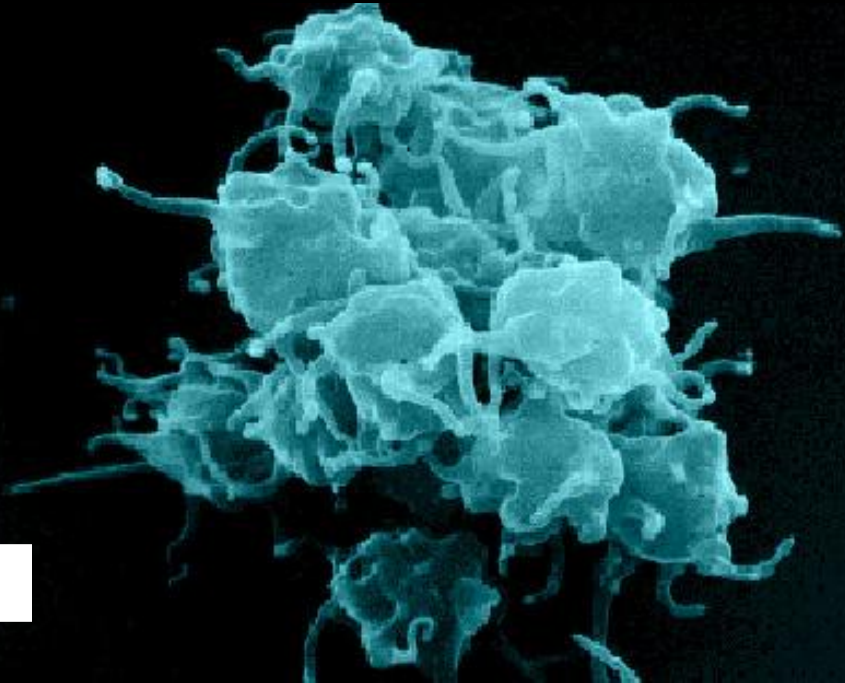
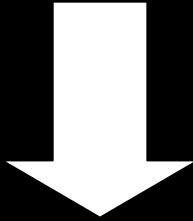
CHEMOFACTORS

**PRO INFLAMMATION
CYTOKINS**





**PLATELET
ACTIVATION**



GROWFACTORS

CHEMOFACTORS

**PRO INFLAMMATION
CYTOKINS**



**ACTIVATED
PLATELET**

**FIGHTING CELLS
MIGRATION
MONOCYTS**

**FIGHTING CELLS
MIGRATION
LEUCOCYTS**

TNF ALPHA

INTERLEUKIN 1

H MACROPHAGE

LEUCOCYTS

INTERLEUKIN 1

INTERLEUKIN 1

**ACTIVATED
PLATELET**

**FIGTHING Cells
MIGRATION
MONOCYTS**

**FIGTHING Cells
MIGRATION
LEUCOCYTS**

TNF ALPHA

INTERLEUKIN 1

H MACROPHAGE

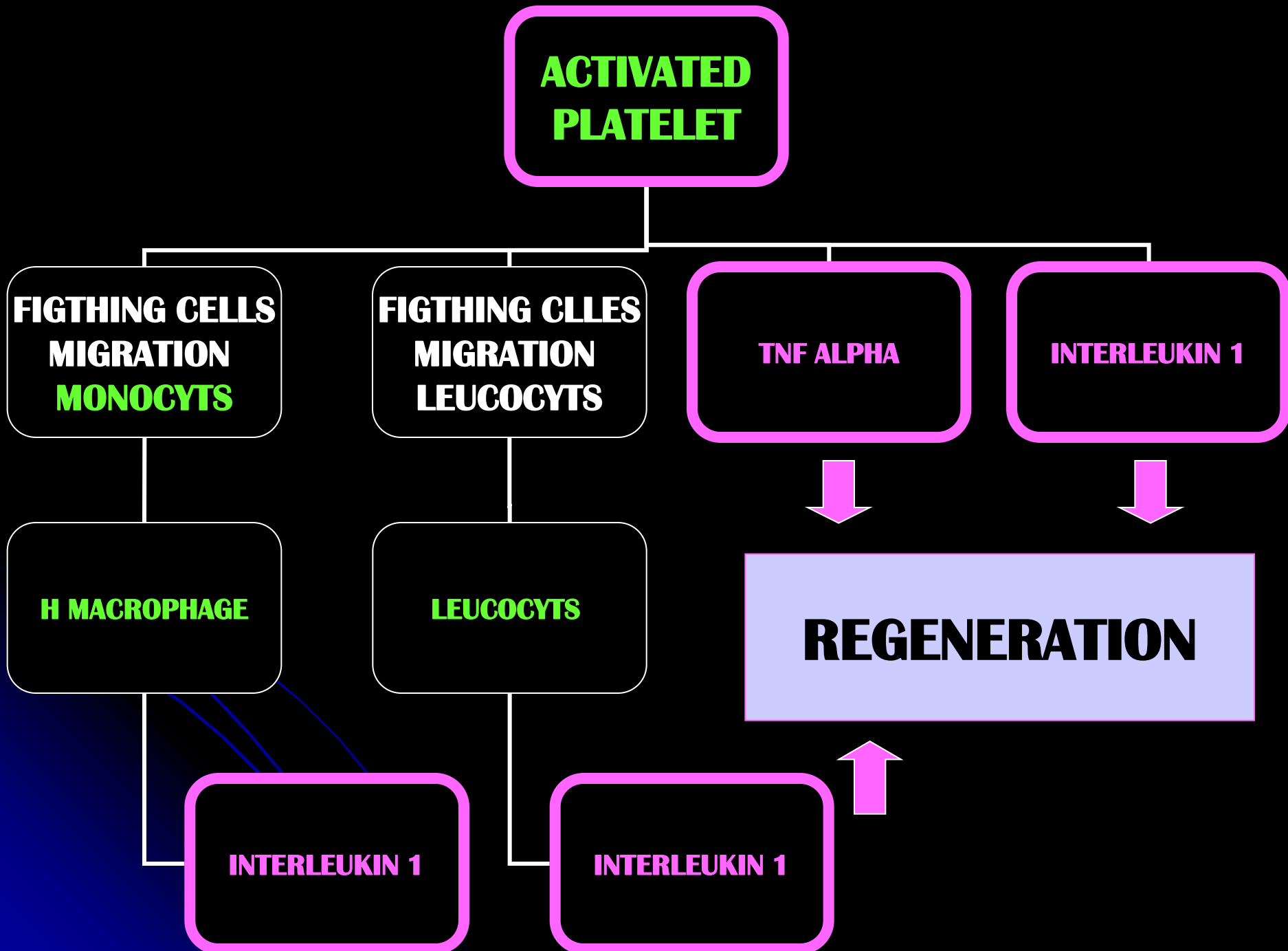
LEUCOCYTS

**STEMM CELLS
DIFFERENTIATION
STIMULATION**

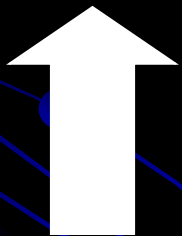
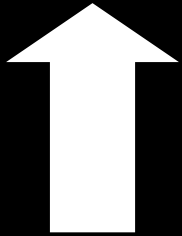
**FIBROBLAST
LOCAL
POPULATION
GROWTH
STIMULATION**

INTERLEUKIN 1

INTERLEUKIN 1



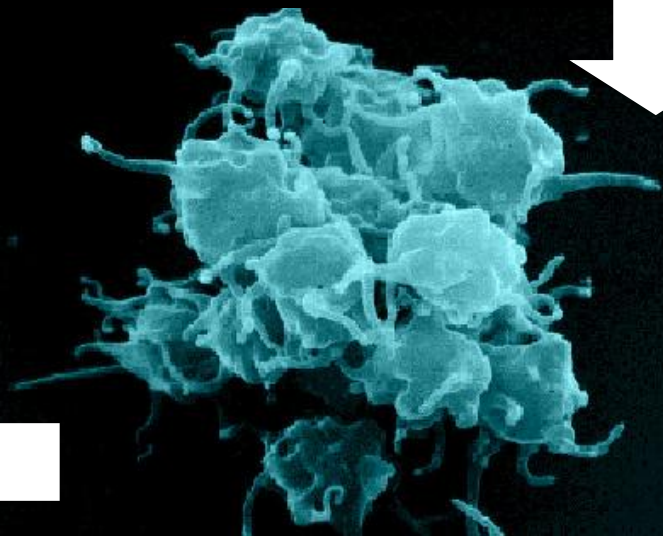
**INFLAMMATION
REGENERATION**



COAGULATION

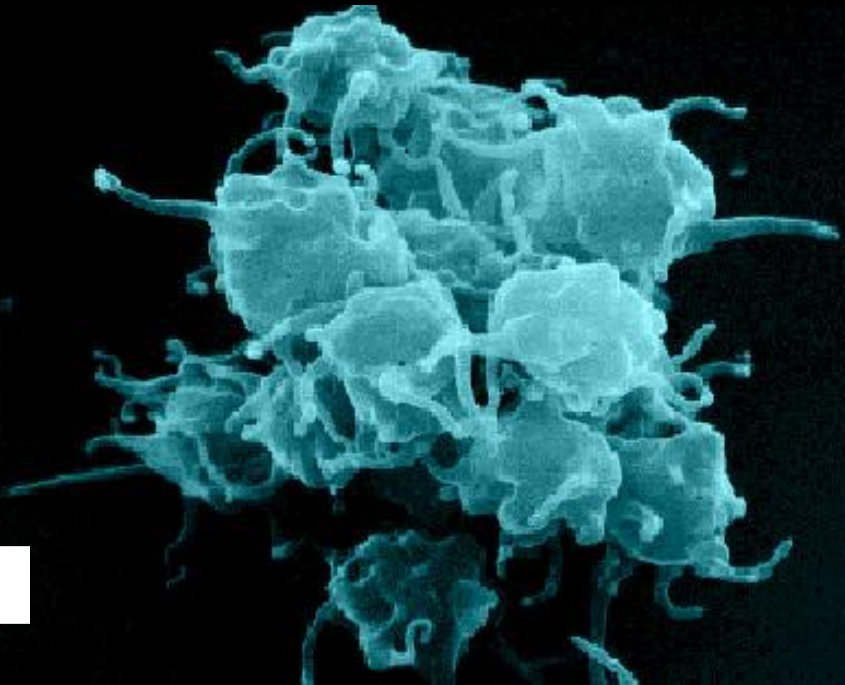
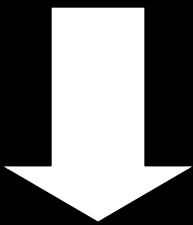


PLATELET ACTIVATION





**PLATELET
ACTIVATION**



GROWFACTORS

CHEMOFACTORS

**PRO INFLAMMATION
CYTOKINS**



**ACTIVATED
PLATELET**

**FIGTHING CELLS
MIGRATION
MONOCYTS**

**FIGTHING CELLS
MIGRATION
LEUCOCYTS**

TNF ALPHA

INTERLEUKIN 1

H MACROPHAGE

LEUCOCYTS

**HYSTIOCYT
MACROPHAGE**

**LEUCOCYTS
LYMPHOCYTS**

**ACTIVATED
PLATELET**

**FIGHTING CELLS
MIGRATION
MONOCYTS**

**FIGHTING CELLS
MIGRATION
LEUCOCYTS**

TNF ALPHA

INTERLEUKIN 1

H MACROPHAGE

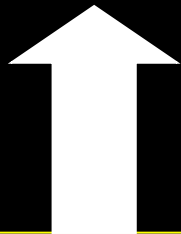
LEUCOCYTS

ANTIBIOTIC

**HYSTIOCYT
MACROPHAGE**

**LEUCOCYTS
LYMPHOCYTS**

ANTIBIOTIC REGENERATION



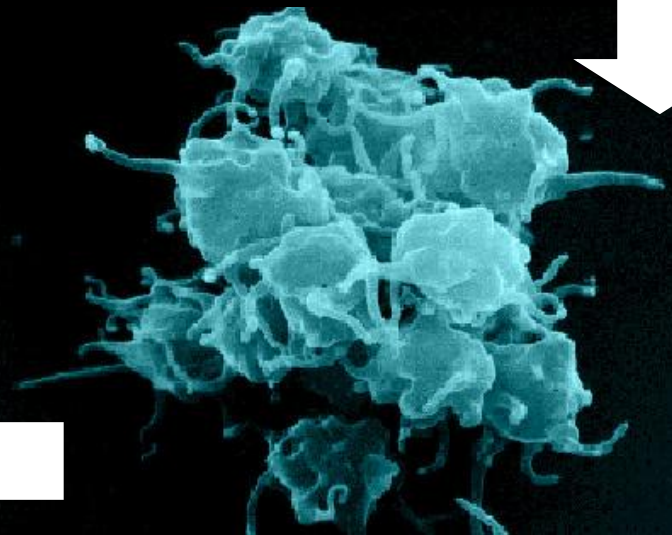
MIGRATION

**MONOCYT
LEUCOCYT**

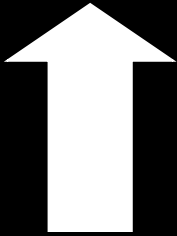
CHEMOFACTORS



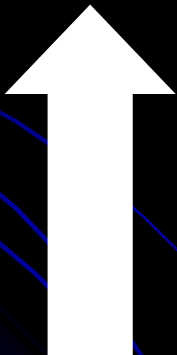
PLATELET ACTIVATION



PAIN KILLER ACTION



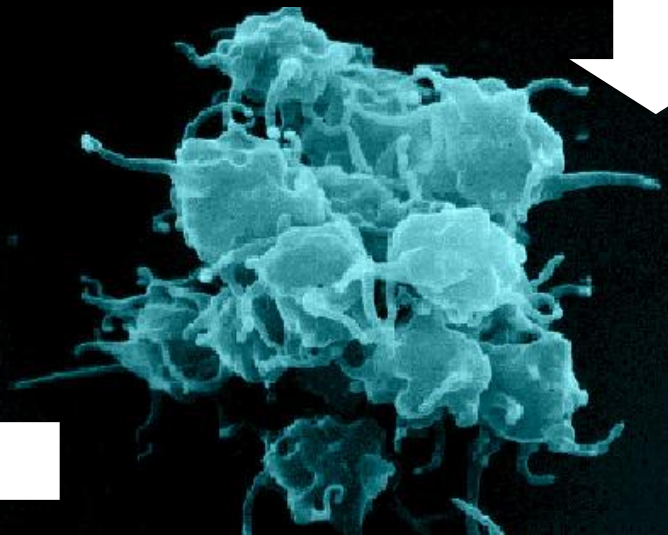
ENDORPHINE PRODUCTION



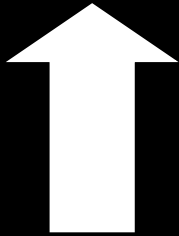
CHEMOFACTORS



PLATELET ACTIVATION



ANTI INFLAMMATORY ACTION



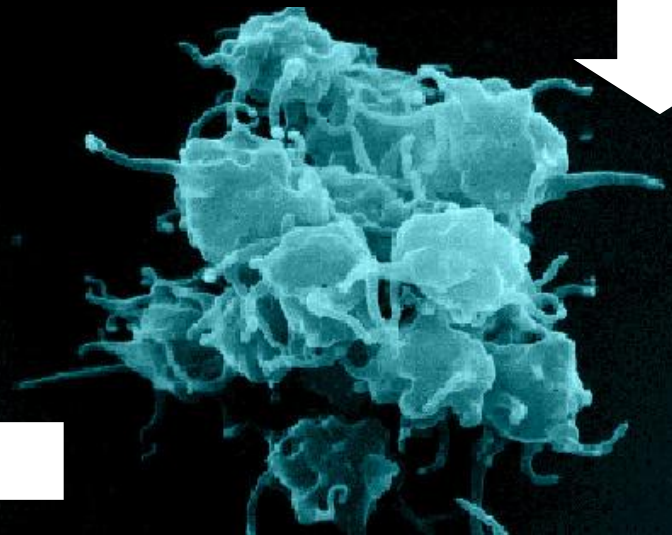
Interleukin 1 inhibition
INTERLEUKIN 6
TGF B



CHEMOFACTORS

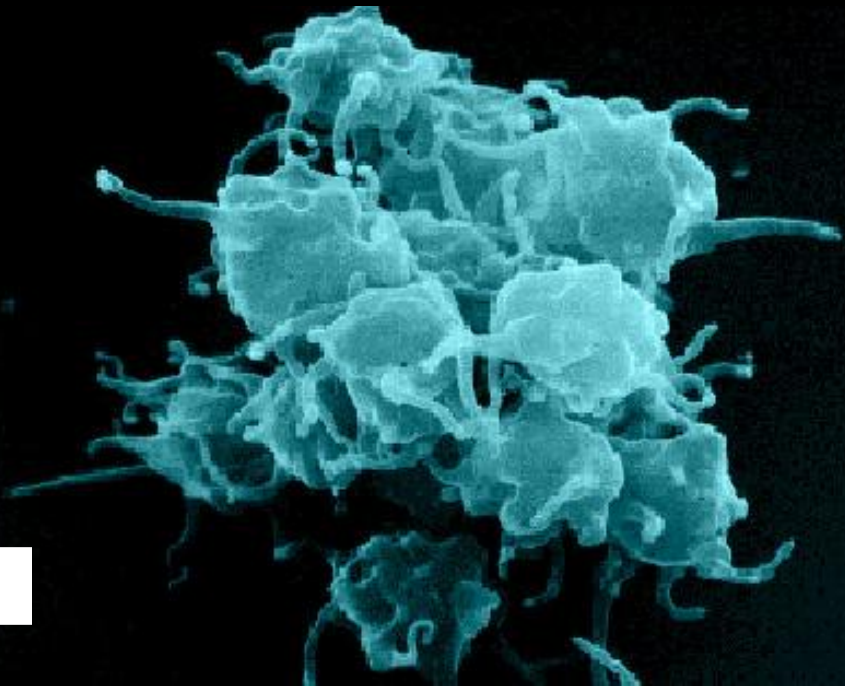
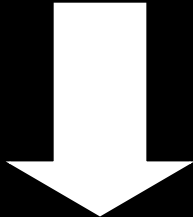


PLATELET ACTIVATION





**PLATELET
ACTIVATION**



GROWFACTORS

CHEMOFACTORS

**PRO INFLAMMATION
CYTOKINS**



- **PDGF** (AA-AB-BB-CC), chemotactic for cells migration and enhance proliferation of fibroblasts and ECM production.
- **FGF** (fibroblast G. F.) migration, mitogenic , proliferation (Fb,Kc)
- **KGF** : keratinocyte growth factor
- **EGF** mitogenic
- **TGF a-b** strong upregulation of the wound early after injury, hemostasis...
- **VEGF**, stimulate angiogenesis
- **PLGF & Angiopoietin**, stimulate angiogenesis
- **IGF**, insulin growth factor mitogenesis in autocrine manner
- **Scatter Factors** (Plasminogen-related factor)
- **HGF** (Hepatocyte G.F.)
- **NGF** (Nerve G.F.)
- **ACTIVINS** (TGF family) differentiation several cells & tissues
- **Chemokines** Chemo-attractive cytokines,
- **IL1 IL6 IL10 TNF**, proinflammatory cytokines
- **Granulocyte-macrophage** colony stimulating factor
- **Leptin** (stimulate adipocytes)
- **BMP 2-4-7** etc..... PDGF : platelet derived growth factor
- **TGF-alpha & beta** : transforming growth factor alpha & beta
- **EGF** : epidermal growth factor
- **PDEGF** : platelet derived epidermal growth factor
- **PDAF** : platelet derived angiogenesis factor
- **IL-8** : interleukine – 8
- **TNF-alpha** : tumor necrosi factor alpha
- **CTGR** : connective tissue growth factor
- **GM-CSF** : granulocyte macrophage colony growth factor

- **PDGF (AA-AB-BB-CC)**, chemotatic for cells migration and enhance proliferation of fibroblasts and ECM production.
- **FGF** (fibroblast G. F.) migration, mitogenic , proliferation (Fb,Kc)
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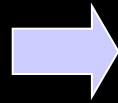
- **FGF (fibroblast G. F.)** migration, mitogenic , proliferation (Fb,Kc)
- **KGF : keratinocyte** growth factor
- **Leptin** (stimulate adipocytes)
- **VEGF**, stimulate angiogenesis
- **NGF (Nerve G.F.)**



SKIN REGENERATION

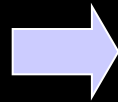
SKIN

- EPIDERMIS



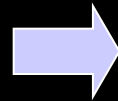
- KERATINOCYTE

- DERMIS



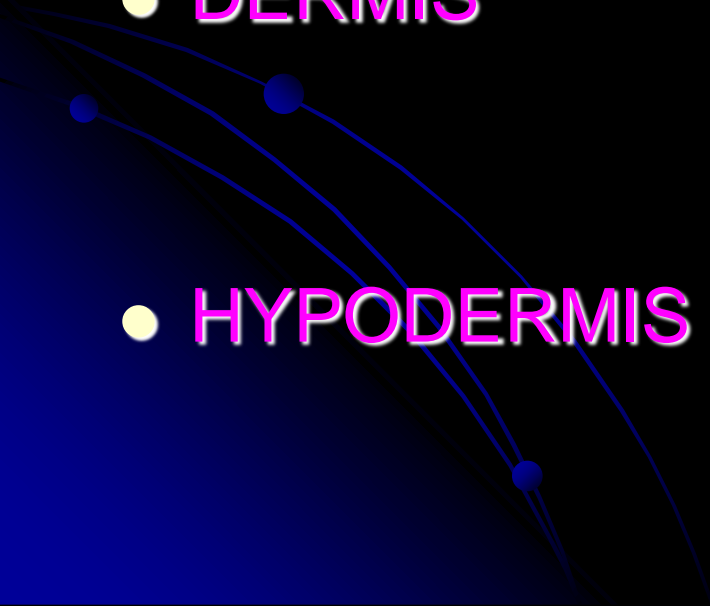
- FIBROBLAST

- HYPODERMIS



- FIBROBLAST

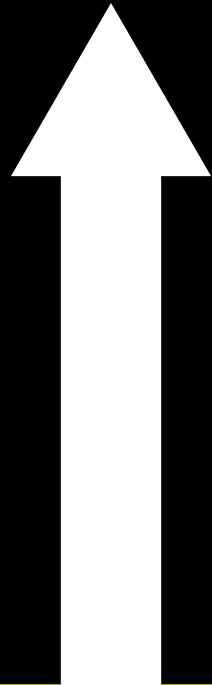
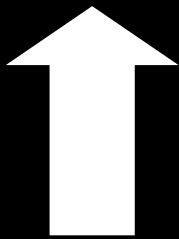
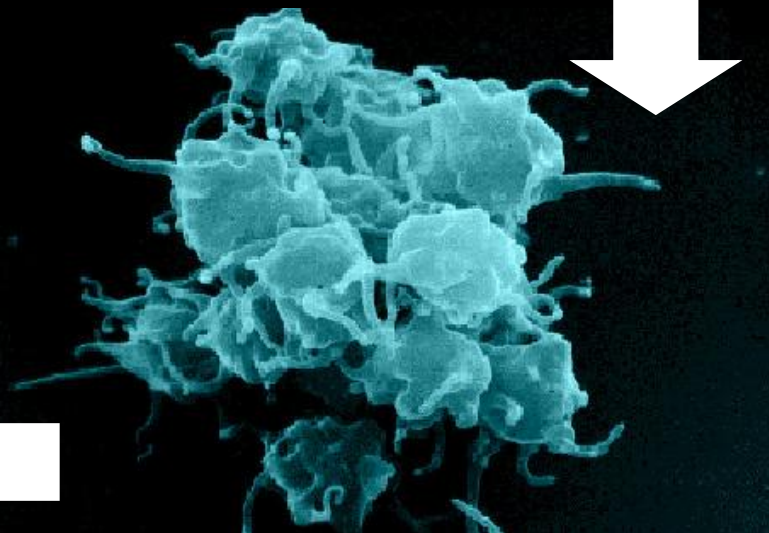
- ADIPOCYTE



LOCAL FIBROBLAST KERATINOCYT ADIPOCYT POPULATION STIMULATION And REGENERATION



PLATELET ACTIVATION



**FIBROBLAST
KERATINOCYTE
ADIPOCYTE
MIGRATION**

GROW FACTORS

CHEMOKINES



STEMM CELLS DIFFERENTIATION And GENERATION

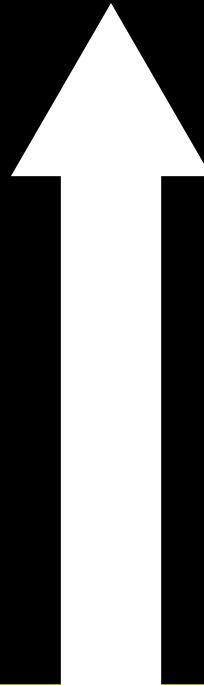
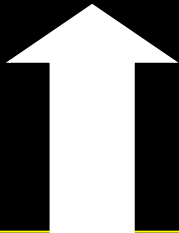
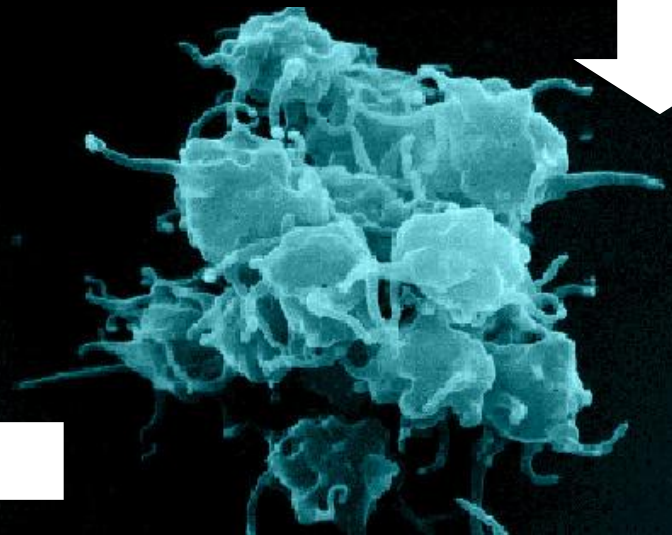
MIGRATION

STEMM CELLS

GROW FACTORS

CHEMO FACTORS

PLATELET ACTIVATION



Regeneration

DIRECT Regeneration

- Fibroblast growth
- Keratinocyt growth
- Adipocyt growth
- Vascular growth
- Nervs growth

INDIRECT Regeneration

- Stemm cells growth
- Stemm cells differentiation
- Stemm Cells growth factors (Fibroblats)

**MESENCHYMALES
STEM
CELLS**

```
graph TD; A[MESENCHYMALES STEM CELLS] --- B[Anti Apoptotical Factors]; A --- C[Chemo Factors]; A --- D[Growth factors];
```

**Anti
Apoptotical
Factors**

**Chemo
Factors**

**Growth
factors**

- Adrénomédulline **ADM** Cytoprotection
- Angio-associated migratory protein **AAMP** Angiogenèse
- Angiogénine **ANG** Angiogenèse, prolifération cellulaire
- Angiopoïétine-1 **AGPT1** Migration cellulaire, stabilisation cellulaire
- Bone-morphogenetic protein-2 **BMP2** Développement
- Bone-morphogenetic protein-6 **BMP6** Différenciation cellulaire, croissance
- **Connective tissue growth factor CTGF** Angiogenèse, croissance cellulaire
- Endothéline-1 **EDN1** Cytoprotection, prolifération cellulaire
- **Fibroblast growth factor-2 FGF2** Prolifération cellulaire, migration
- **Fibroblast growth factor-7 FGF7** Prolifération et stabilisation cellulaire
- Hepatocyte growth factor **HGF** Cytoprotection, angiogenèse, migration
- Insuline-like growth factor-1 **IGF-1** Cytoprotection, migration, contractilité
- Interleukine 1 **IL-1** Stimulation de VEGF
- Interleukine 6 **IL-6** Stimulation de VEGF
- Interleukine 11 **IL-11** Cytoprotection
- Kit ligand/stem cell factor **KITLG (SCF)** Prolifération et migration cellulaire
- Leukemia inhibitory factor **LIF** Prolifération cellulaire, cytoprotection
- Macrophage migration inhibitory factor **MIF** Prolifération cellulaire, réponse inflammatoire

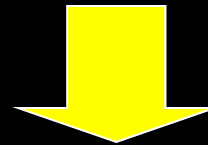
- Métalloprotéase-1 **MMP-1** Dégradation de la matrice, formation de tubule
- Métalloprotéase-2 **MMP-2** Dégradation de la matrice, formation de tubule
- Métalloprotéase-9 **MMP-9** Dégradation de la matrice
- Monocyte chemoattractant protein-1 **MCP-1** Migration des monocytes
- Macrophage-specific colonystimulating factor **M-CSF** Prolifération et migration des monocytes
- Placenta growth factor **PGF** Prolifération cellulaire
- Plasminogen activator **PA** Dégradation des molécules de la matrice
- Platelet-derived growth factor **PDGF** Prolifération et migration cellulaire
- Pleiotrophine **PTN** Prolifération cellulaire
- Secreted frizzled-related protein-1 **SFRP1** Développement
- Secreted frizzled-related protein-2 **SFRP2** Développement
- Stem cell-derived factor-1 **SDF-1** « Homing » des progéniteurs cellulaires
- Thrombospondine-1 **THBS1** Migration cellulaire
- Thymosine- β 4 **TMSB4** Migration cellulaire, cytoprotection
- Tissue inhibitor of metalloproteinase-1 **TIMP-1** Migration cellulaire
- Tissue inhibitor of metalloproteinase-2 **TIMP-2** Migration cellulaire
- Transforming growth factor- β **TGF- β** Maturation des vaisseaux, prolifération
- Tumor necrosis factor- α **TNF- α** Dégradation de la matrice, prolifération
- Vascular endothelial growth factor **VEGF** Cytoprotection, prolifération, migration, angiogenèse

- **Interleukine 1 IL-1**
Stimulation de VEGF
- **Interleukine 6 IL-6**
Stimulation de VEGF
- **Tumor necrosis factor- α TNF- α**
Dégradation de la matrice, prolifération



**STEM CELLS
DIFFERENTIATION**

- **Fibroblast growth factor-2 FGF2**
Prolifération cellulaire, migration
- **Fibroblast growth factor-7 FGF7**
Prolifération et stabilisation cellulaire

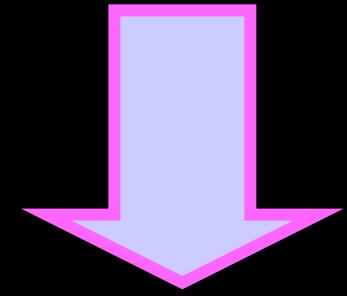


**FIBROBLAST
POPULATION
GROWTH**



**HEALING PROCESS
CELLS PRODUCTION**

AUTOCRIN STIMULATION
PDGF TGF b



INTERLEUKIN
PRO INFLAMATION
CYTOKIN

FIBROBLAST
PRODUCTION

PLATELET
BASIC FIBROBLAST
GROW FACTOR

STEM CELLS
GROW FACTORS

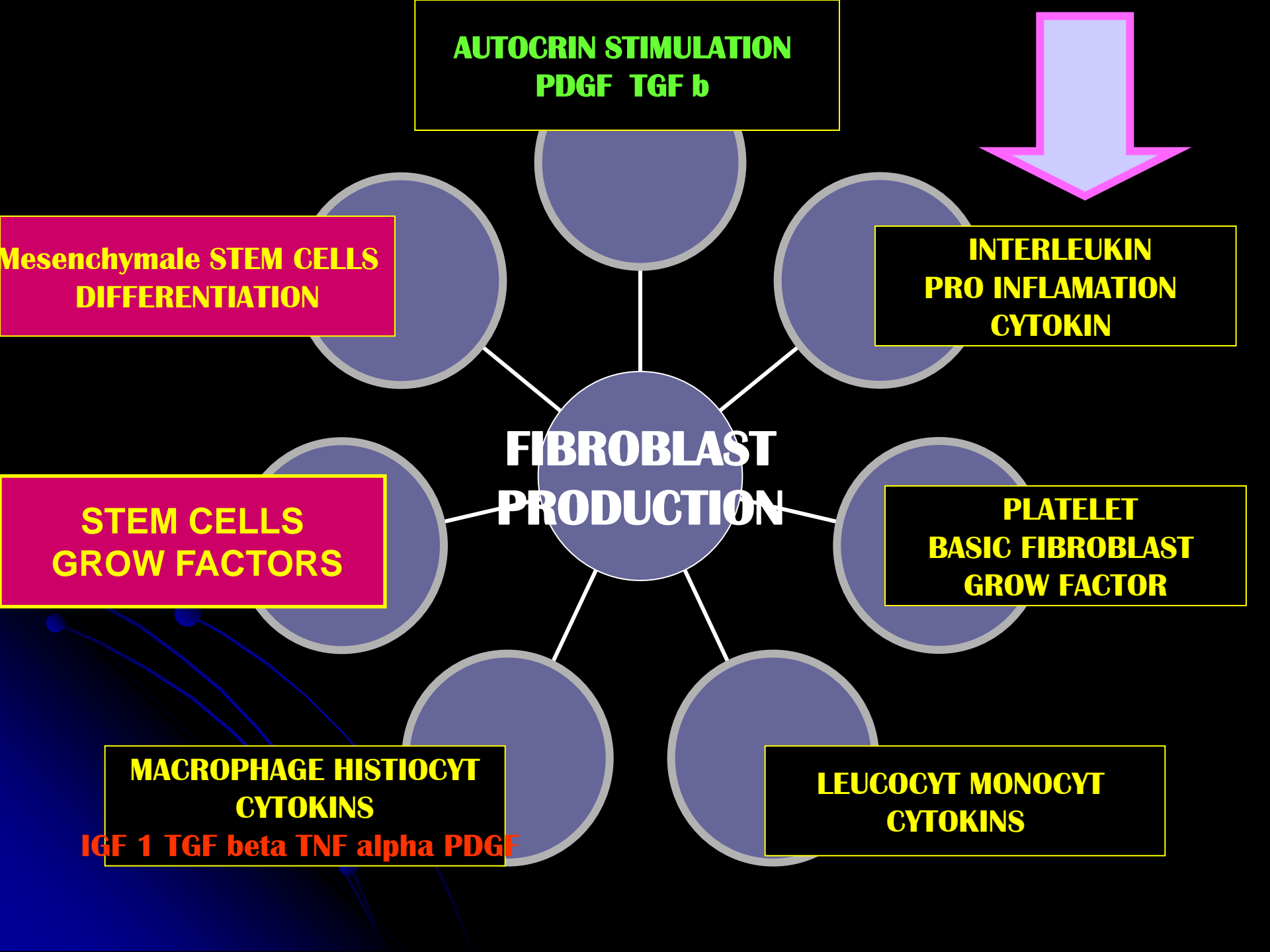
LEUCOCYT MONOCYT
CYTOKINS

MACROPHAGE HISTIOCYT
CYTOKINS

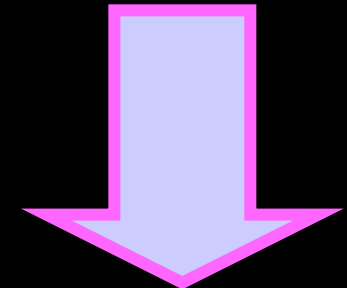
IGF 1 TGF beta TNF alpha PDGF

Mesenchymale STEM CELLS
DIFFERENTIATION

STEM CELLS
GROW FACTORS



AUTOCRIN STIMULATION
TGF A TGF B



Mesenchymale STEM CELLS
DIFFERENTIATION

INTERLEUKIN
PRO INFLAMATION
CYTOKIN

KERATINOCYT
PRODUCTION

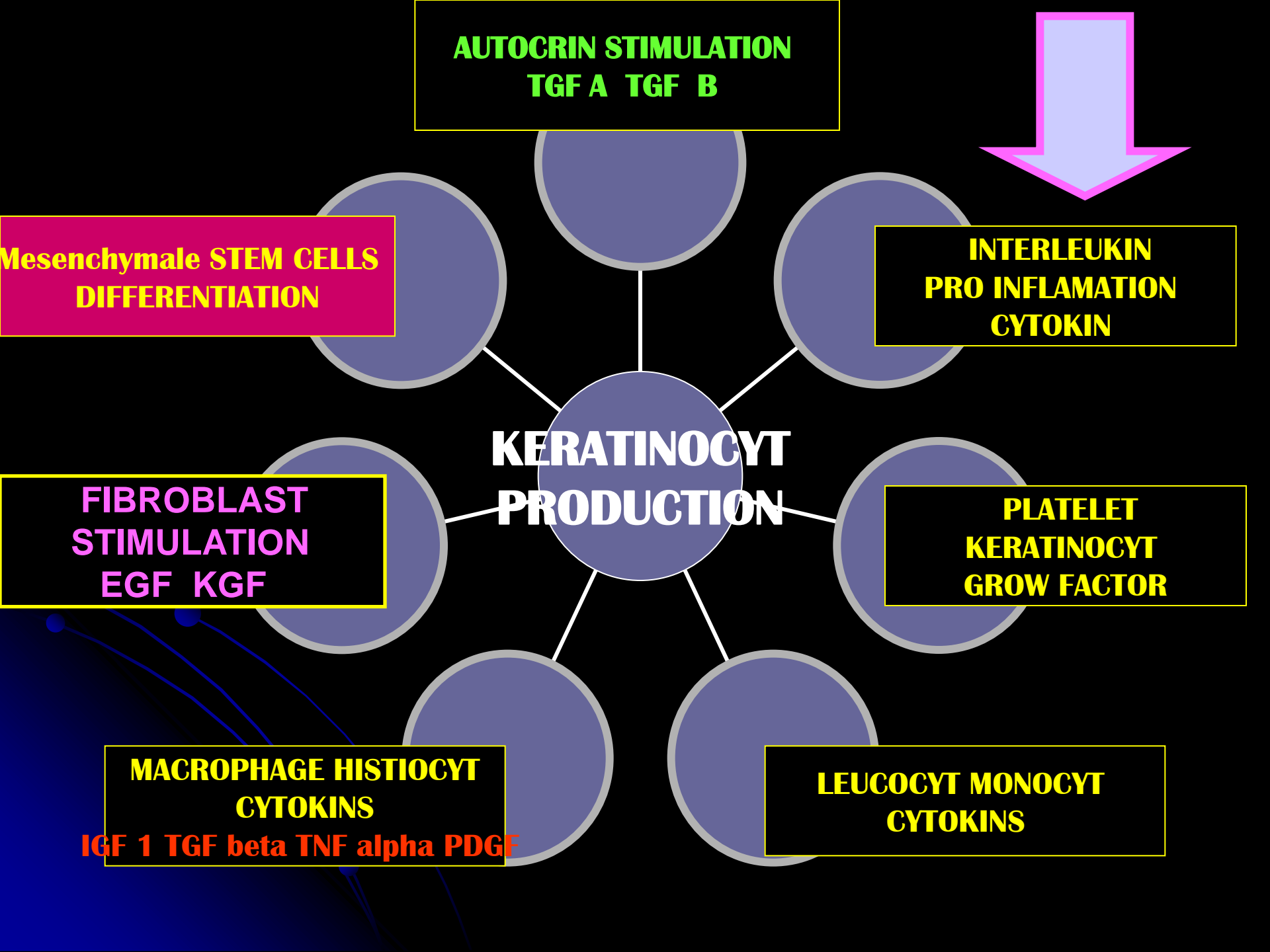
FIBROBLAST
STIMULATION
EGF KGF

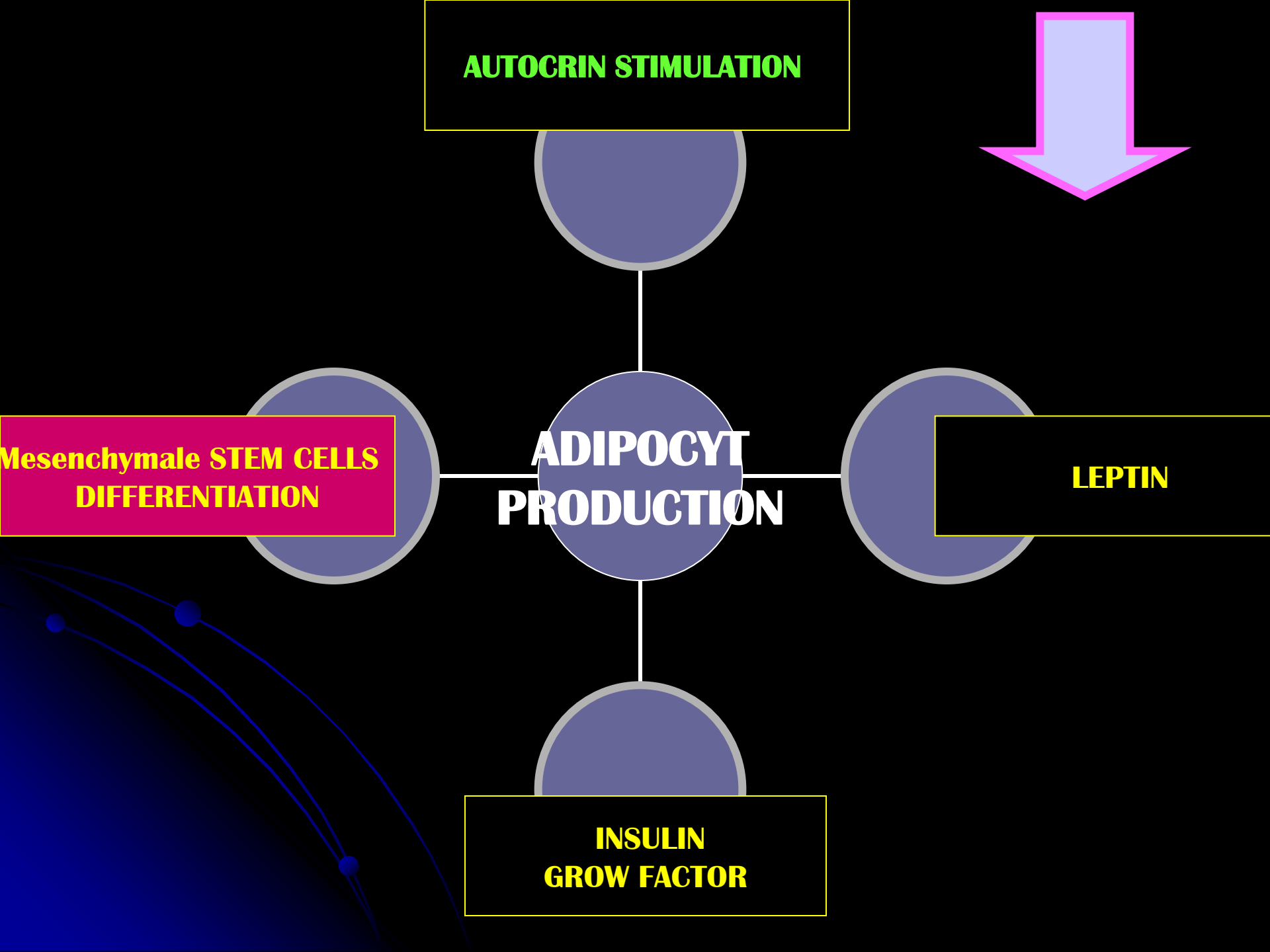
PLATELET
KERATINOCYT
GROW FACTOR

MACROPHAGE HISTIOCYT
CYTOKINS

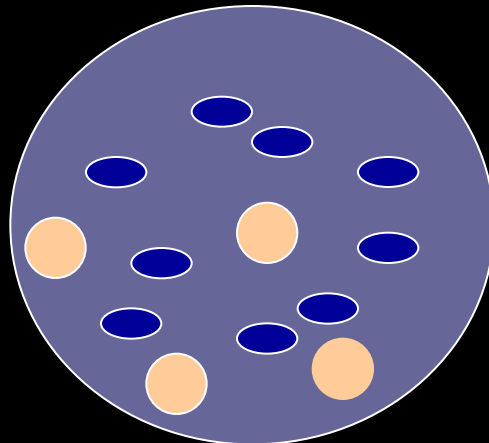
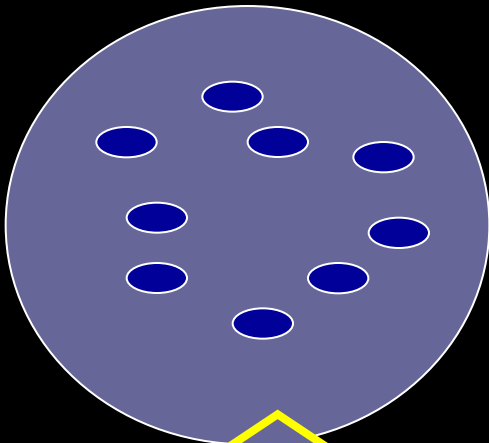
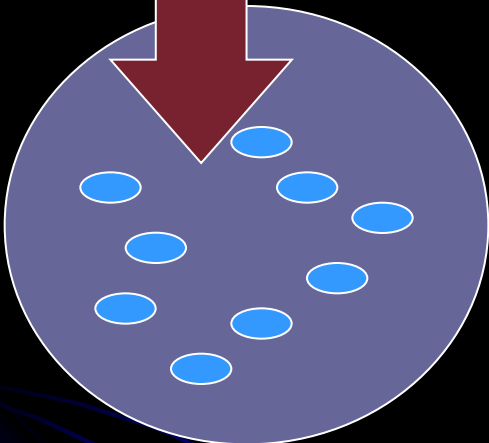
LEUCOCYT MONOCYT
CYTOKINS

IGF 1 TGF beta TNF alpha PDGF

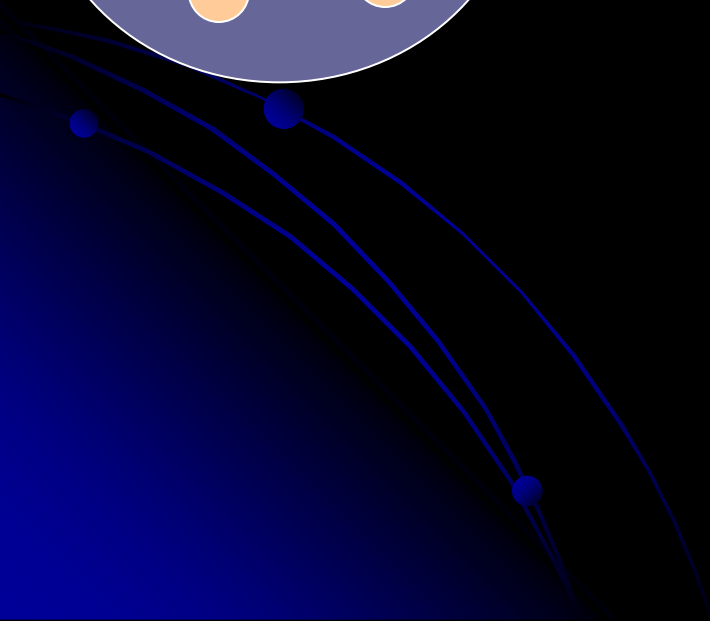
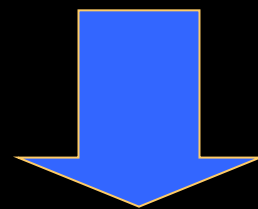
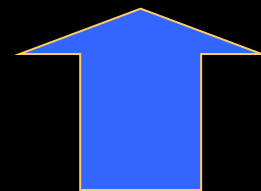
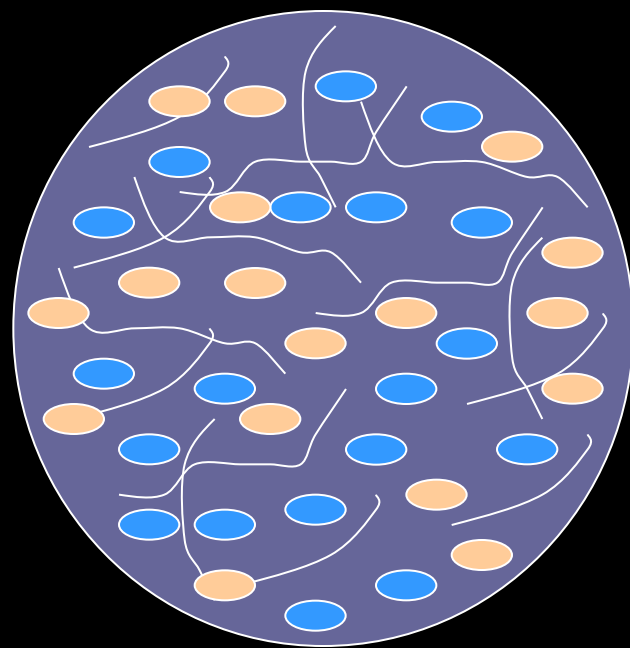
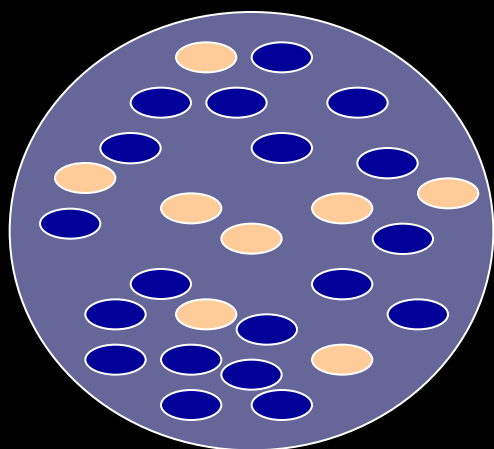
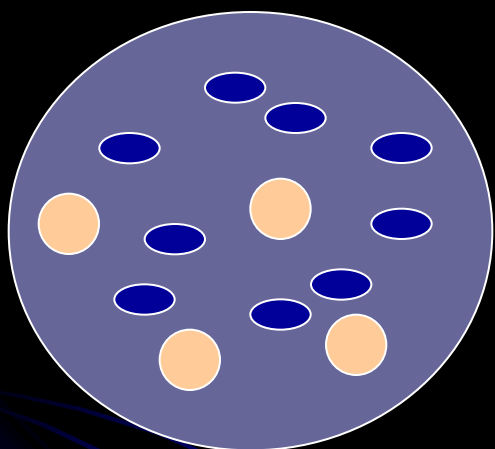


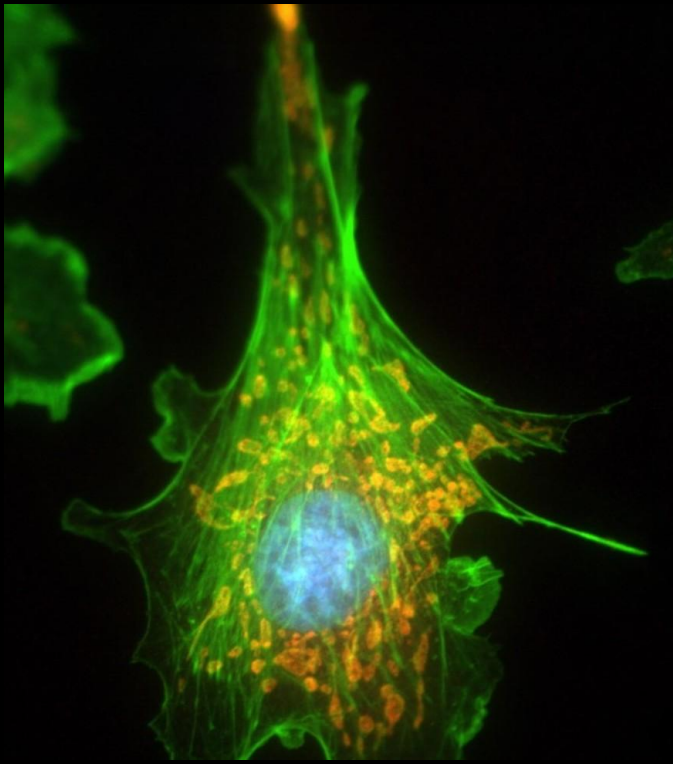


**PLATELET
RICHED
PLASMA**

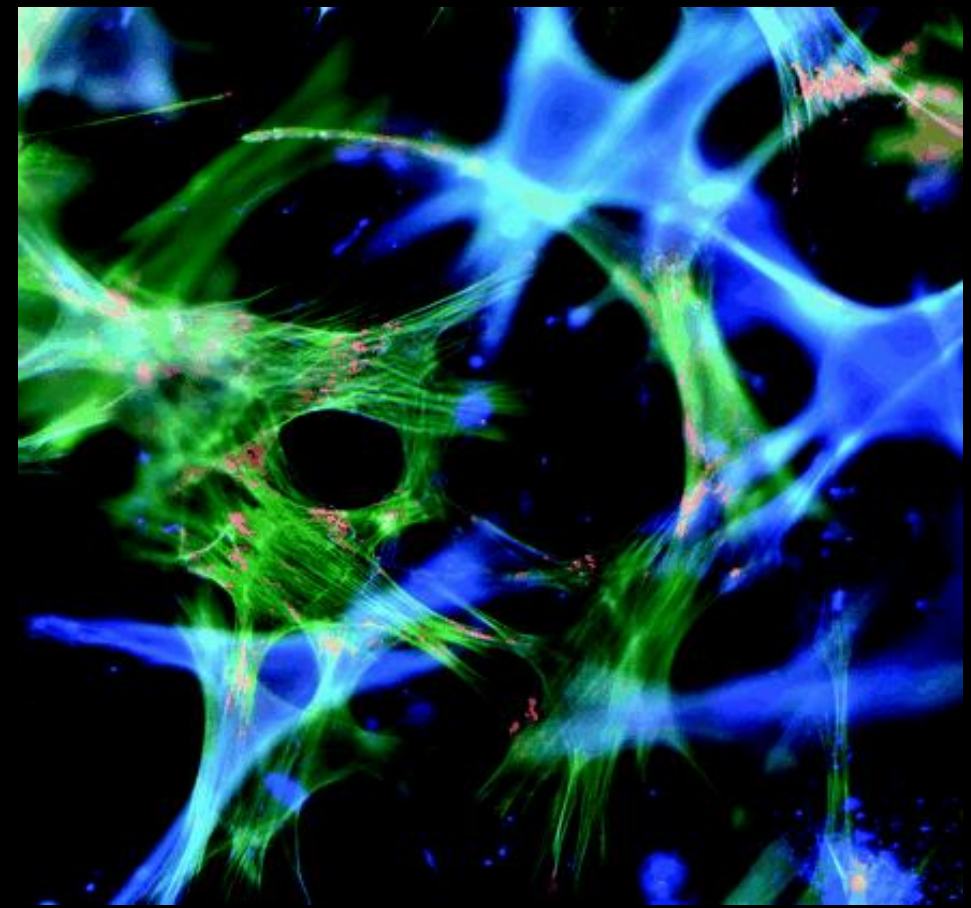
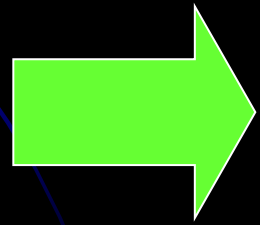


STEMM CELLS





DAY 5



MYOSIN



CASE REPORTS

PRP Medical Procedure

- Blood20 ml
- Material selection2 types
- Trade Mark
.....
- Dermo hypodermic Injection
- 0,05 to 0,1 ml per 2 square cm
- Needle 0,30 mm / 23 (30 G)



CASE REPORT 1







CASE REPORT 2





DAY 17



CASE REPORT 3



15/4/2011 11:47



19/4/2011 13:49

DAY 4



CASE REPORT 4

Burn : 3 degree



11 CM



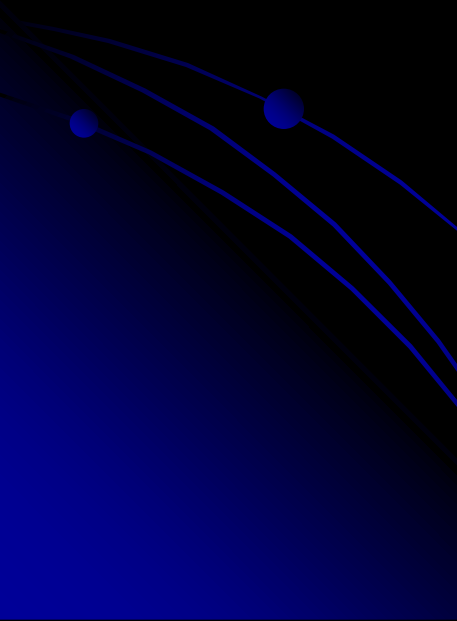








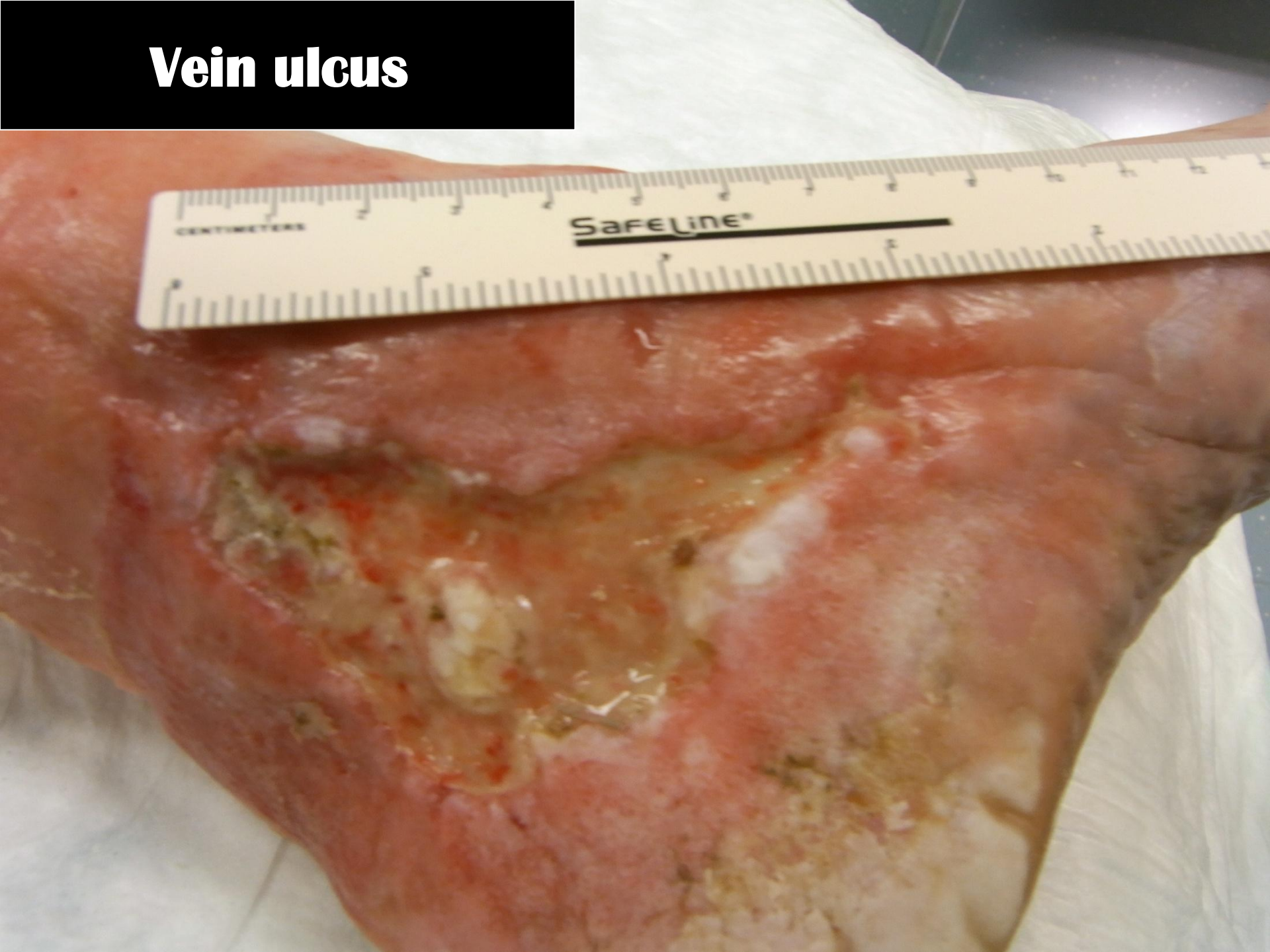
Day 45 - 50





CASE REPORT 5

Vein ulcer





DAY 12



CASE REPORT 6

Amputation and diabetes



**8 Months
after operation**





DAY 21



CASE REPORT 7





DAY 120



Après injection



Day 2

Flammazine cream



DAY 3



DAY 4



DAY 6



DAY 12



DAY 20





DAY 27





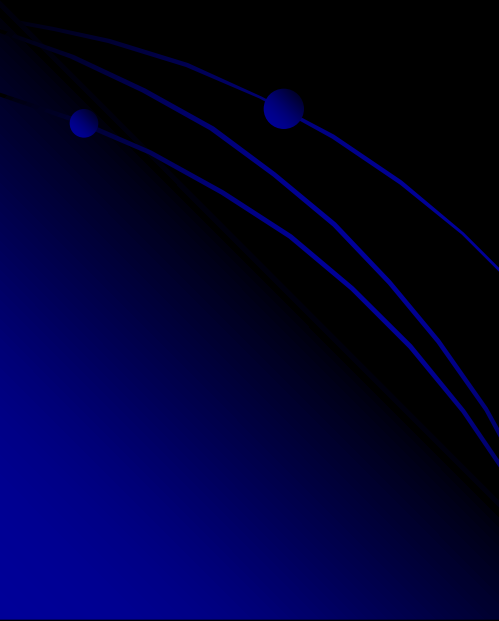
DAY 55

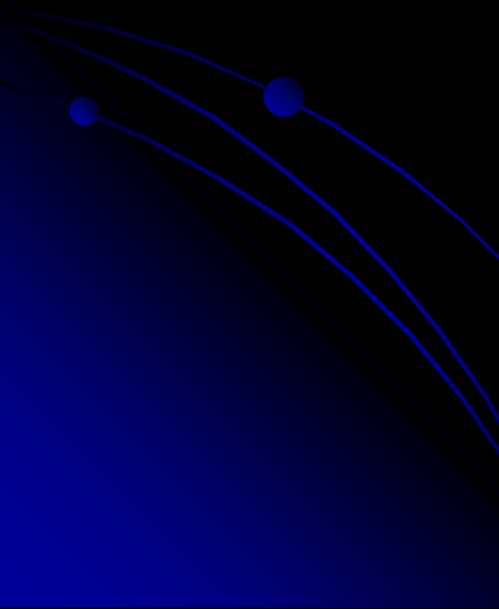


DAY 70



CASE REPORT 8







DAY 55



CASE REPORT 9







DAY 45



DIABETIS .
Physiopathology

CICATRISATION

DIABETIS

Modifications système neurovégétatif
Shunts artériolo-veinulaires

Atteintes
sensitives

diminution
phagocytose
et chimiotactisme

Retards
de
cicatrisation

Hypoxie
cutanée
secondaire

Remaniements
des zones
d'appui

Risque
infectieux
accru

- **Faulty Initiation of Proteoglycan Synthesis Causes Cardiac and Joint Defects**
- **Sevjidmaa Baasanjav, Lihadh Al-Gazali, Taishi Hashiguchi, Shuji Mizumoto, Bjoern Fischer, Denise Horn, Dominik Seelow, Bassam R. Ali, Samir A.A. Aziz, Ruth Langer, Ahmed A.H. Saleh, Christian Becker, Gudrun Nürnberg, Vincent Cantagrel, Joseph G. Gleeson, Delphine Gomez, Jean-Baptiste Michel, Sigmar Stricker, Tom H. Lindner, Peter Nürnberg, Kazuyuki Sugahara, Stefan Mundlos, and Katrin Hoffmann**

**Proteoglycans in cancer biology, tumour
microenvironment and angiogenesis.**

lozzo RV, Sanderson RD.

**Some of the small leucine-rich
proteoglycans, such as DECORIN and
LUMICAN , act as tumour repressors by
physically antagonizing receptor tyrosine
kinases**

Proteoglycans and signal transduction

Cellular functions of proteoglycans—an overview

Norbert Perrimon and Merton Bernfield

- Two major families of cell surface HSPGs, **SYNDECANS** and **GLYPICANS**, have been identified.
- These bind a multitude of growth factors and extracellular matrix molecules, and **have been implicated in several signal transduction pathways that regulate cell proliferation and cell shape.**



**DIABETIS .
FRENCH BALANCE
OF ACCOUNTS**

EPIDEMIOLOGY

- 285 millions en 2010
- **PREVALENCE** 6,6 %
- Pays les plus touches

INDE

CHINE

ETATS UNIS

BRESIL

ALLEMAGNE

- # 500 millions en 2030

EPIDEMIOLOGY

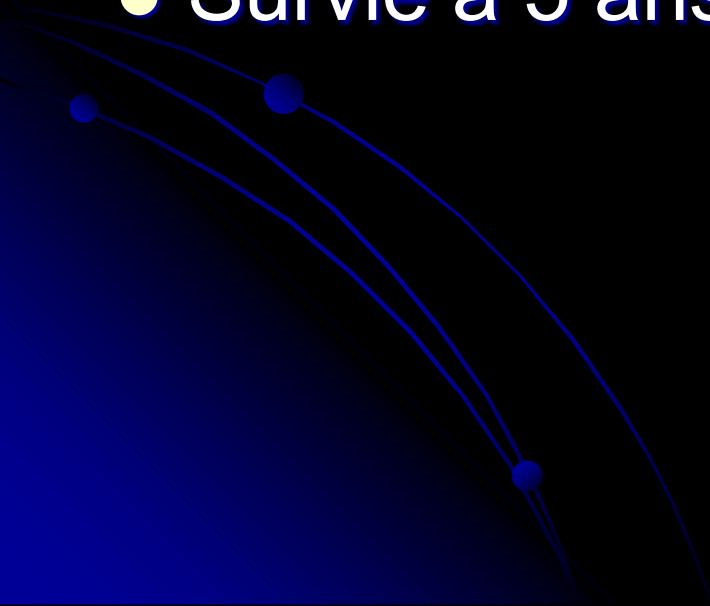
- **12 à 15% des diabétiques** présentent ou ont présenté une plaie du pied .
- Cette prévalence augmente avec l'âge, puisqu'elle peut atteindre plus de 15% après 80 ans.

EPIDEMIOLOGY

- Le risque d'amputation15% des diabétiques vont subir une amputation au cours de leur vie.
- Taux par an en France8000
(données PMSI 2003.)

EPIDEMIOLOGY

- Taux de ré-amputation**56% à 5 ans**
- Survie à 5 ans**40 à 50%.**



ECONOMY

- Plaie **10 000 et 20 000 Euros.**

Cout pour 6,6% Populat..... **59 600 000 000**

- Amputation .. **32 000 Euros.**

Cout pour 8000ion **256 000 000**

- Ces dépenses sont liées pour une grande part au nombre et à la durée des hospitalisations qui progresse de 8 % par an pour une durée moyenne de séjour de 18 jours.

PLAIES ULCERES DIABETIQUES

TRAIT CLASSIQUE

10000
25000

INVALIDITE
DOULEURS

POLYPATHOLOGIE
DECUBITUS

AMPUTATION
32000

PRP
PANSEMENT HUMIDE

1500
2000

DIMINUTION
+ + + +

AMBULATOIRE

0 %

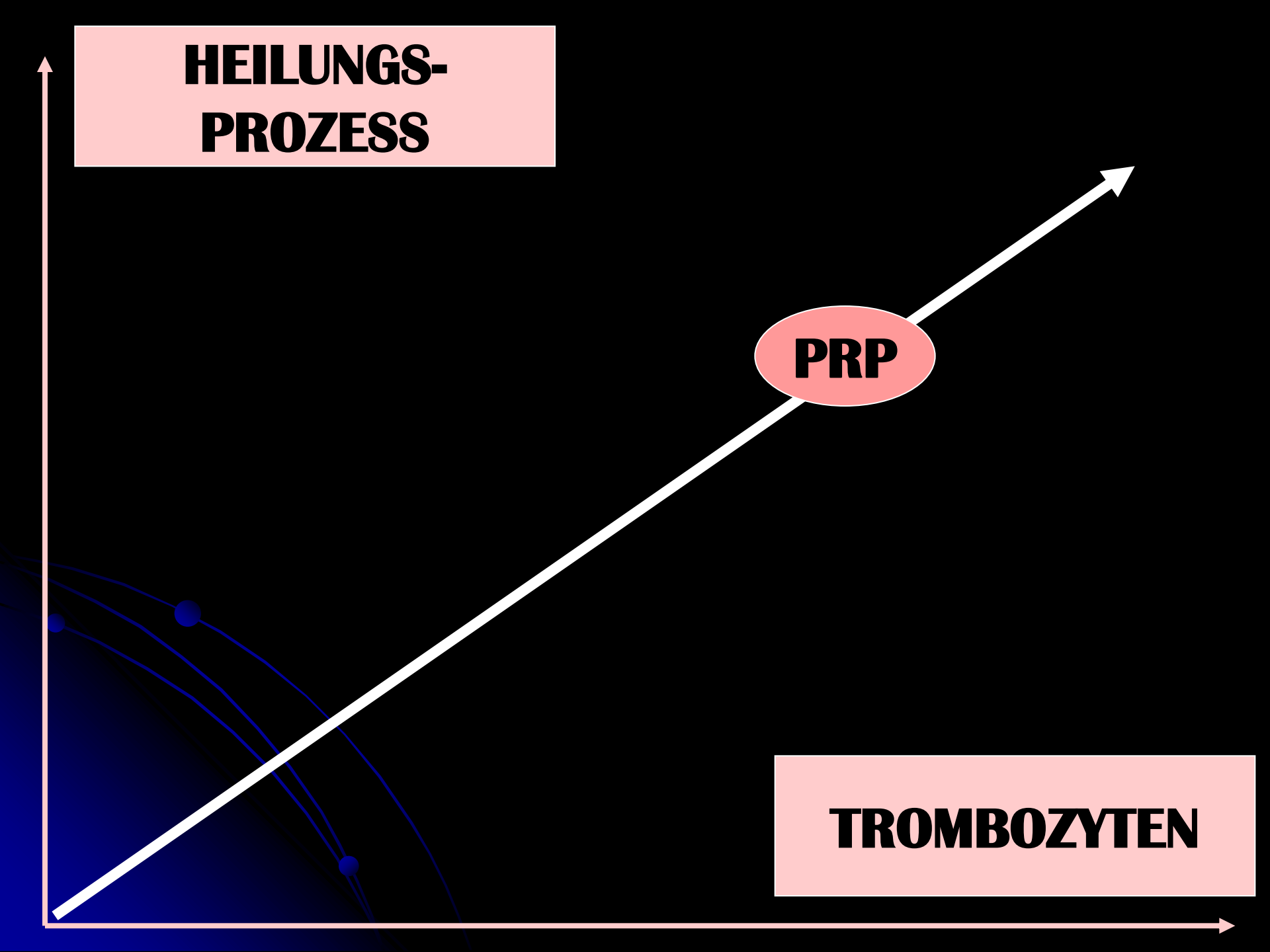


**P.R.P.
THERAPY**

**HEILUNGS-
PROZESS**

PRP

TROMBOZYTEN





250 %

- **Effects of Platelet-Rich Plasma on Intestinal Anastomotic Healing in Rats: PRP Concentration is a Key Factor**

Ryushiro Yamaguchi, M.D.,¹ Hideo Terashima, M.D., Ph.D., Satoshi Yoneyama, M.D., Sosuke Tadano, M.D., Ph.D., and Nobuhiro Ohkohchi, M.D., Ph.D.

- Department of Surgery, Graduate School of Comprehensive Human Sciences, University of Tsukuba, Tsukuba, Ibaraki, Japan



P.R.P.
AUTO IMMUNITY

AUTOIMMUNITY

- Tumor Necrosis Factor Alpha **TNF alpha** cytokines
Base of immun Aktivation (LYMPHO TH 2)



- **Interleukin 17**



- **Lymphocyte Th17** 2008
lignée des lymphocytes T CD4 (dits auxiliaires)
Cytokines Pro-inflammation cytokin (*IL-17*)



- **Interleukin 1**



- **Mesenchymale stammzellen stimulation immunoreduktion**





**P.R.P.
MALPRACTICE**

COMPLICATIONS / MALPRACTICES

INDICATIONS

- ORTHOPEDIE
- RHUMATOLOGIE
- DIABETOLOGIE
- DERMATOLOGIE
- ESTHETIQUE
- RECONSTRUCTION

> 1200 PATIENTS

6 YEARS

0 %



**P.R.P.
LAWS**

Union europeene

- **DIRECTIVES**

- **DIRECTIVE 2009/120/CE du 14 septembre 2009
DE LA COMMISSION EUROPEENNE**

- **modifiant la directive 2001/83/CE du Parlement
européen et du Conseil instituant un code
communautaire relatif aux médicaments à usage
humain en ce qui concerne les médicaments de
thérapie innovante**

- **(Texte présentant de l'intérêt pour l'EEE)**

EUROPEEN COMMISSION
DIRECTIV 2009/120/CE
14 sept 2009

BUNDESGESETZ

BUNDES-
ARTZKAMMER

TÜV
DEUTCHLAND

OFFICIAL NATIONAL
IMPORT DEALER

DOCTOR

DRG SYSTEM

HOSPITAL

DIRECTIVES

- **INJECTABLE POUR L'ETRE HUMAIN**

- **B 2 CLASS**

- **NORMES EMPAQUETAGE ET DE STERILISATION**

- **C E NORMS**

- **ISO 11607- 1**

- **ISO 11607- 2**



THANK YOU FOR YOUR ATTENTION

