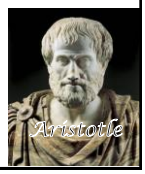
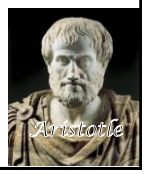
We are what we repeatedly do; excellence, then, is not an act but a habit.



With regard to excellence, it is not enough to know, but we must try to have and use it.



Principles of Periodontal Tissue Engineering

Dr. Ahmad Abdel Salam Hamdan
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Department of Oral & Maxillofacial Surgery, Oral Medicine, & Periodontology
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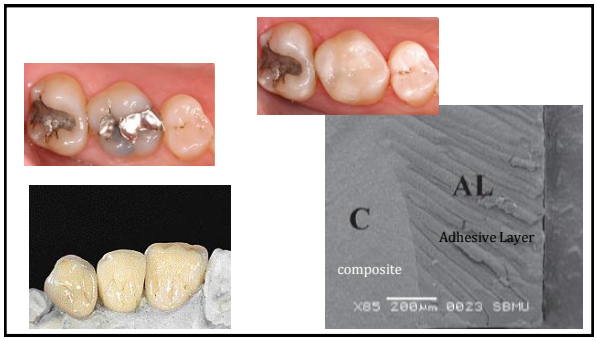
University of Jordan

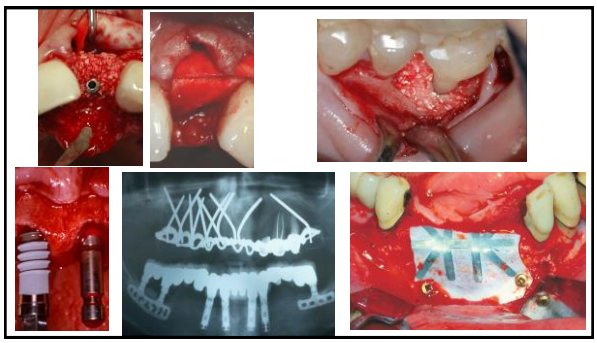


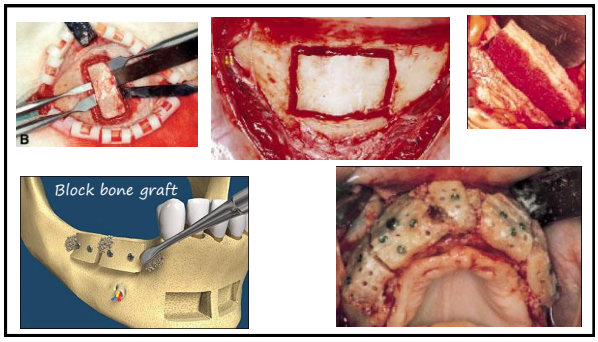
Goldberg M.
In vitro and in vivo studies on the toxicity of dental resin components: a review. Clin Oral Investig. 2008 Mar;12(1):1-8.

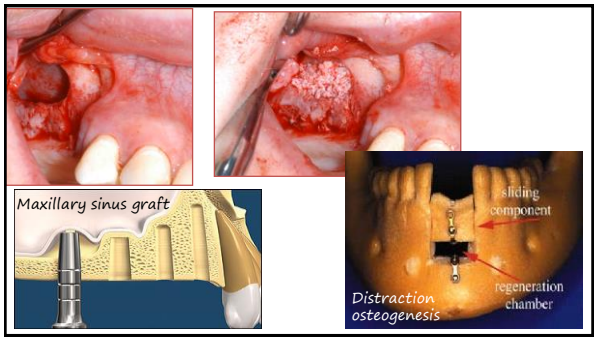
« There is a large gap between the results published by research laboratories and clinical reports »

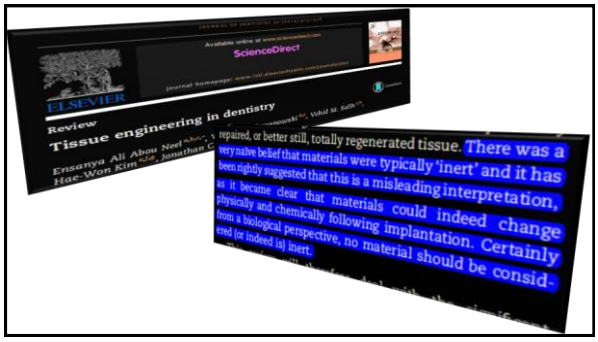
Schweikl H, Spagnuolo G, Schmalz G.
Genetic and cellular toxicology of dental resin monomers. J Dent Res. 2006 Oct;85(10):870-7.

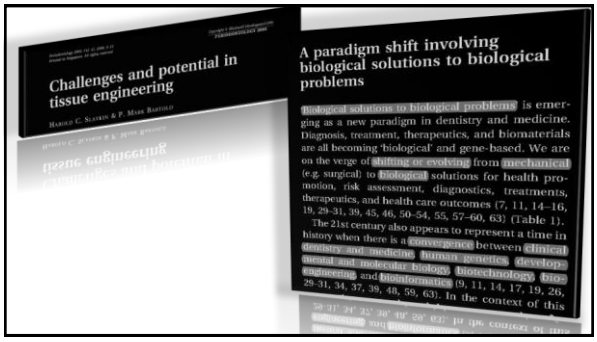
« Cytotoxicity and genotoxicity of some of these methacrylates have been identified in a vast number of investigations during the last decade »



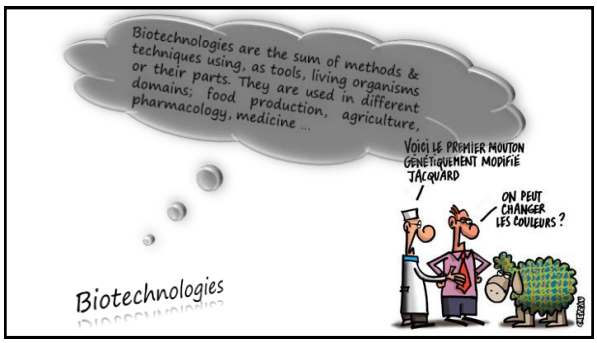

Block bone graft


Maxillary sinus graft
sliding component
regeneration chamber
Distraction osteogenesis


ScienceDirect
Review
Tissue engineering in dentistry
repaired, or better still, totally regenerated tissue. There was a very naïve belief that materials were typically 'inert' and it has been rightly suggested that this is a misleading interpretation, as it became clear that materials could indeed change physically and chemically following implantation. Certainly from a biological perspective, no material should be consid-


Challenges and potential in tissue engineering
A paradigm shift involving biological solutions to biological problems
Biological solutions to biological problems is emerging as a new paradigm in dentistry and medicine. Diagnosis, treatment, therapeutics, and biomaterials are all becoming 'biological' and gene-based. We are on the verge of shifting or evolving from mechanical (e.g. surgical) to biological solutions for health promotion, risk assessment, diagnostics, treatments, therapeutics, and health care outcomes (7, 11, 14–16, 19, 29–31, 39, 45, 46, 50–54, 55, 57–60, 63) (Table 1).
The 21st century also appears to represent a time in history when there is a convergence between clinical dentistry and medicine, human genetics, developmental and molecular biology, biotechnology, bioengineering, and bioinformatics (9, 11, 14, 17, 19, 26, 29–31, 34, 37, 39, 48, 59, 63). In the context of this


ScienceDirect
Review
Tissue engineering in dentistry
composition are briefly considered here.
There has been a clear and distinct hypothetical shift in regenerative medicine from using medical devices and whole tissue grafts, to a more explicit approach that utilises specific bioactive, biodegradable synthetic or natural scaffolds combined with cells and/or biological molecules, to create a functional replacement tissue in a diseased or damaged site. Every era in medical research over the past 50 years, involving the use of biomaterials in order to replace tissue function, has been distinct and identified by particular developmental successes and materials. For example, in the 1950s, there was a predominant use of metal implants and associated devices with little thought offered to the effects on local tissues, let alone the cells. Throughout the '70s and '80s, there was a significant increase in the use of polymers and synthetic materials where researchers considered both biological and material properties. More recently, there has been a distinct and concentrated effort in the design and use of both natural and degradable scaffolds and advanced biological consideration of the materials.

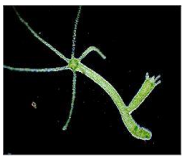

Biotechnologies are the sum of methods & techniques using, as tools, living organisms or their parts. They are used in different domains: food production, agriculture, pharmacology, medicine ...
Biotechnologies
VOICI LE PREMIER MOUTON GÉNÉTIQUEMENT MODIFIÉ JACQUARD
ON PEUT CHANGER LES COULEURS ?

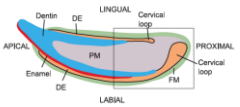
Biotechnologies in medicine

Tissue Regeneration

What is

REGENERATION ???





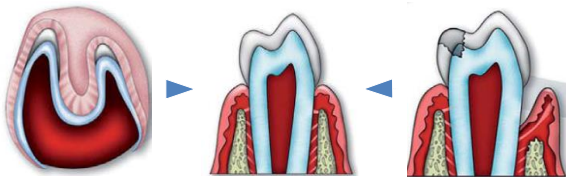
WHAT IS REGENERATION?

WHAT IS REGENERATION?

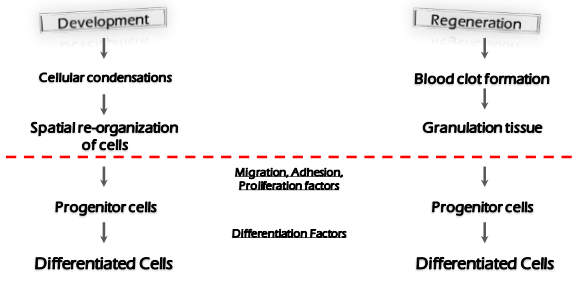
IT IS NOT TO HAVE AN ENDLESS LIFE

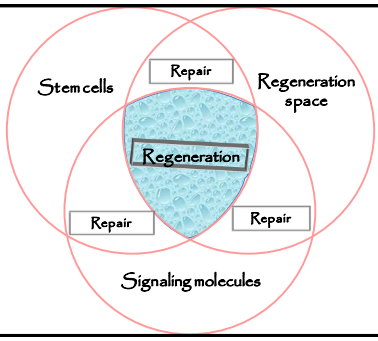
WHAT IS REGENERATION?

The restoration of the morphology and the function of damaged or lost tissues, in a way similar to that occurring during development.



Regeneration… The principle





Regeneration… Tissue Engineering

Interdisciplinary domain involving biological sciences & principles of engineering aiming to develop biological substitutes in order to restore, maintain, & ameliorate tissue function & morphology.

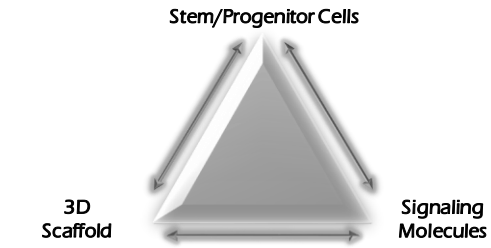
Regeneration… Tissue Engineering

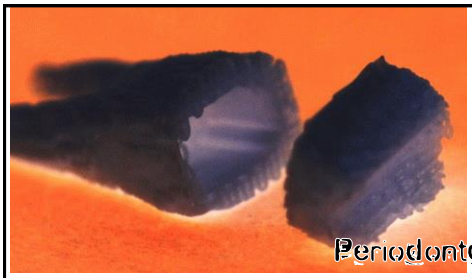
It is an approach that utilizes specific biodegradable synthetic or natural scaffolds as well as advanced molecular techniques in order to replace tissue function.

Regeneration… Tissue Engineering

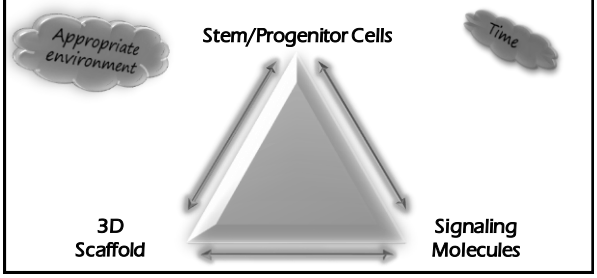
To engineer a **functional biological structure**, cells must be instructed to **differentiate** & **receive positional cues**, & to **synthesize the appropriate ECM molecules** in the **overall shape & dimensions** of the diseased or missing tissues/organs.

Regeneration… Tissue Engineering





Periodontal Tissue Engineering… Components



… Components… Signaling Molecules

rhPDGF

BMPs

FGF-2

EMD

PRP

… Components… Signaling Molecules

	Platelet-derived growth factor	Fibroblast growth factor-2	Bone morphogenetic proteins	Enamel matrix derivative	Transforming growth factor-beta	Insulin-like growth factor-1, 2
Periodontal ligament cells						
Cell proliferation	++	+++	++	++	–	+
Chemotaxis	++	+++	+	++	0	++
Collagen synthesis	+	–	+	+	+	+
Protein synthesis	+	+	+	+	+	+
Matrix gene expression	++	++/–	?	+	+	+

… Components… Signaling Molecules

	Platelet-derived growth factor	Fibroblast growth factor-2	Bone morphogenetic proteins	Enamel matrix derivative	Transforming growth factor-beta	Insulin-like growth factor-1, 2
Cementoblasts						
Cell proliferation	+++	?	–	++	++	++
Chemotaxis	++	?	?	?	?	?
Collagen synthesis	+	?	++	++	+	+
Protein synthesis	+	?	++	++	+	+
Matrix gene expression	+/–	?	++	++/-	+/–	+/–

… Components… Signaling Molecules

	Platelet-derived growth factor	Fibroblast growth factor-2	Bone morphogenetic proteins	Enamel matrix derivative	Transforming growth factor-beta	Insulin-like growth factor-1, 2
Osteoblasts						
Cell proliferation	++	+++	0	++	+++	++
Chemotaxis	+++	+++	+	++	+++	+
Collagen synthesis	0	++	0	+	++	+
Protein synthesis	0	+	ND	+	+/–	0
Matrix gene expression	+/–	++/–	++	++/–	++	++
Alkaline phosphatase synthesis	0	–	++	++	+/–	0

… Components… Signaling Molecules

Short biological half-life

Receptor-binding problems

Stability of carrier system

Cell adhesion

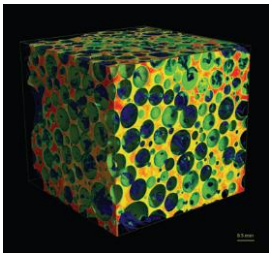
… Components… 3D Scaffold

Autogenous graft

Allograft

Xenograft

Synthetic materials



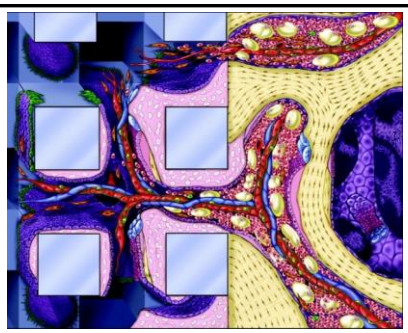
… Components… 3D Scaffold… Role

Provide physical support

Barrier to restrict cell migration in a selective manner

Scaffold for cell migration & proliferation

Serve as time-release mechanism for signaling molecules



… Components… 3D Scaffold

Fibrous inclusion

Problems with resorption

Cell adhesion

Porosity

Oxygen passage

vascularization

… Components… Cells

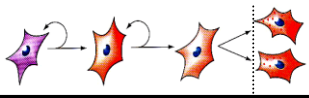
Table 1. Different stem cell populations and their differentiation potential

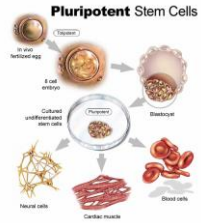
Development stage	Type of stem cell	Differentiation potential
Blastocyst	Embryonic stem cells *Derived from the inner cell mass of the pre-implantation embryo*	Pluripotent
Fetus	Embryonic germ cells *Derived from primordial germ cells isolated from the embryonal gonad*	Pluripotent
Adult	Embryonal carcinoma cells *Derived from primordial germ cells in embryonic gonad and usually found as components of testicular tumors in adults*	Pluripotent
	Adult stem cells *Derived from ectodermal and mesodermal organs of adults*	Multipotent
	Adult cells that have undergone nuclear transformation	Totipotent
	Adult cells that can be induced to an embryonic stem cell phenotype	Inducible pluripotent

… Components… Cells

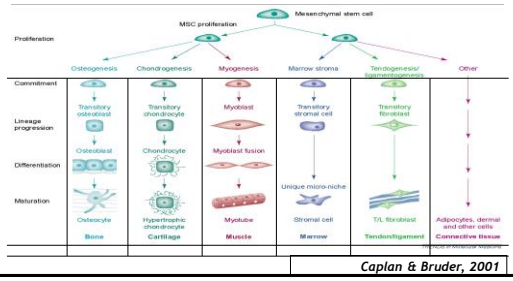
Mesenchymal cells

- **Undifferentiated cells**
- **High proliferation rate over long time**
- **Can differentiate into different cell types**
- **Asymmetrical mitosis**



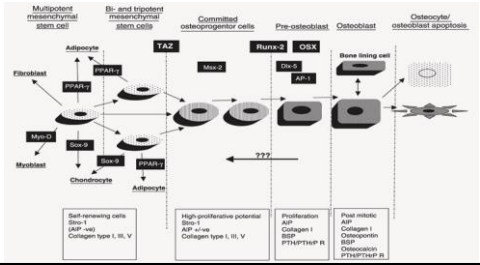


… Components… Cells



Caplan & Bruder, 2001

… Components… Cells



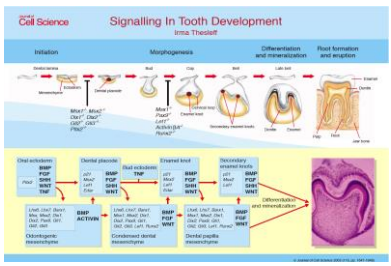
… Components… Cells

- Bone Marrow Stem Cells (BMSC)
- Epithelial Stem Cells (ESC)
- Dental Pulp Stem Cells (DPSC)
- Stem Cells from Exfoliated Deciduous Teeth (SHED)
- Periodontal Ligament Stem Cells (PDLSC)

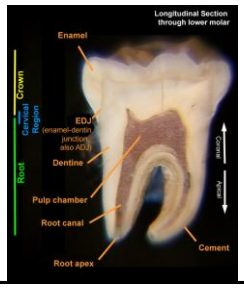
Dental Stem cells….

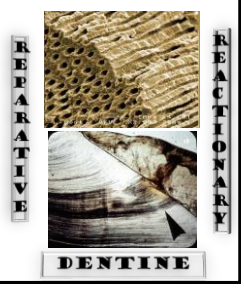
WHY?

… Components… Cells… Dental Stem Cells

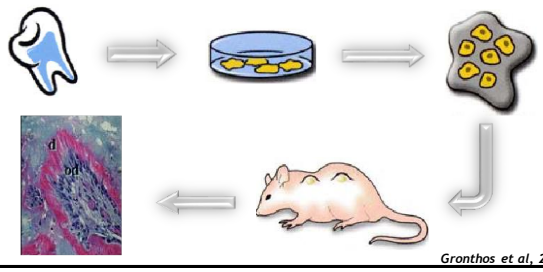


… Components… Cells… Dental Stem Cells



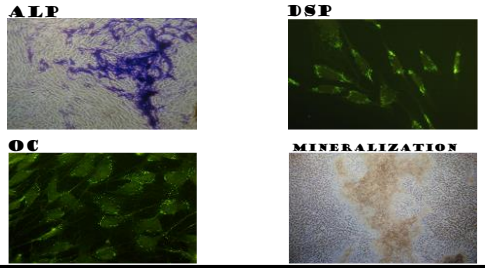


… Components… Cells… Dental Stem Cells



Gronthos et al, 2000

… Components… Cells… Dental Stem Cells



… Components… Cells… Dental Stem Cells

Dental pulp stem cells (DPSCs) *(Gronthos et al, 2000)*

Stem cells from exfoliated deciduous teeth (SHED) *(Miura et al, 2003)*

Periodontal ligament stem cells (PDLSCs) *(Seo et al, 2004)*

Stem cells from apical papilla (SCAP) *(Sonoyama et al, 2006, 2008)*

Dental follicle precursor cells (DFPCs) *(Morsczeck et al, 2005)*

… Components… Cells… Dental Stem Cells

Characteristics

Higher proliferation rate than BMSC under same conditions

Cyclin-dependent Kinase – 6 *(Shi et al, 2001)*

Expression of STRO-1, VCAM-1, α-sma

Heterogenous population

Perivascular niche *(Gronthos, 2000; Shi & Gronthos, 2003)*

… Components… Cells… Dental Stem Cells

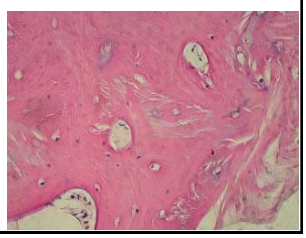
Characteristics

High plasticity

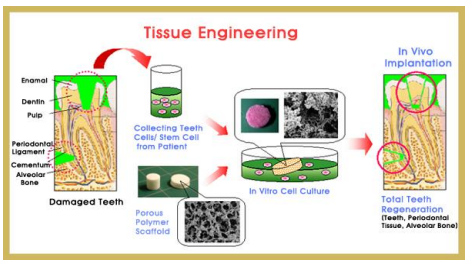
Osteoblasts (Runx2)

Chondroblasts (Sox-9)

Adipocytes (PPARγ)



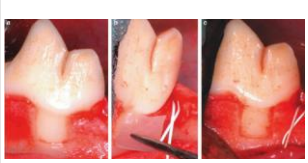
Periodontal Tissue Engineering

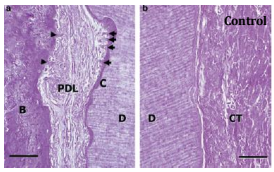


Periodontal Tissue Engineering

Akizuki et al, 2005

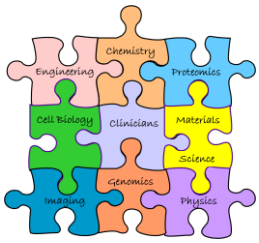
Application of periodontal ligament cell sheet for periodontal regeneration: a pilot study in beagle dogs. *J Periodont Res* 2005; 40: 245-251.





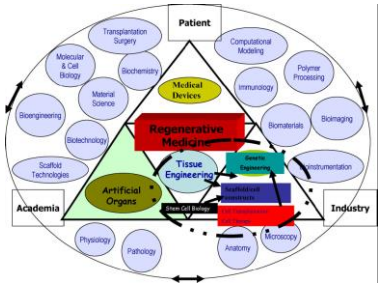
Conclusion...

Conclusion



Conclusion

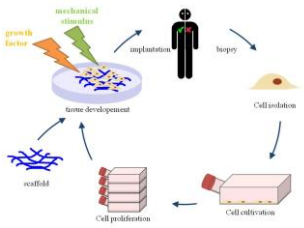
Hutmacher et al, 2007



Conclusion

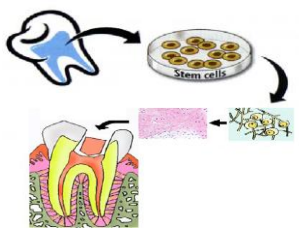
Ex vivo Tissue engineering

In vivo Tissue Engineering



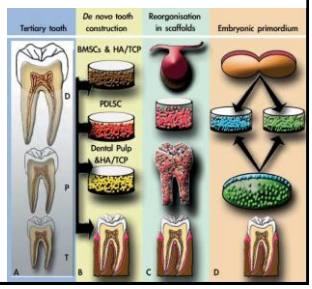
Conclusion

Dentine repair



Conclusion

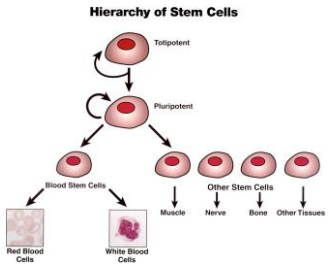
Tooth tissue engineering

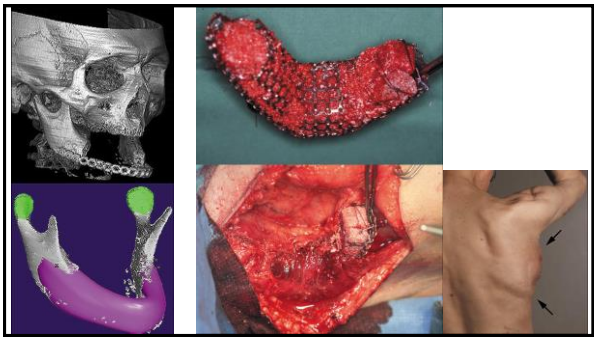


Sartaj et Sharpe, 2006

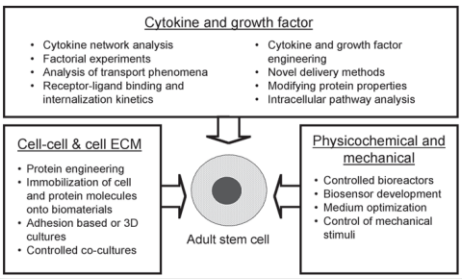
Conclusion

Tissue engineering:
- Bone
- Cartilage
- Nerve
- Muscles





Conclusion… Complexity of TE



Conclusion… Challenges

Biological challenges
- GF
- Signaling pathways
- Root development

Conclusion… Challenges

Technical challenges
- Culture conditions
- Xenogenic products
- Timing
- Ideal scaffold
- Delivery system

Conclusion… Challenges

- Clinical challenges
  - Immunogenic rejection
  - Oncogenic properties
  - Functional integration

Thank you…