Clinical applicability of adipose-derived stem cells in vascular biology

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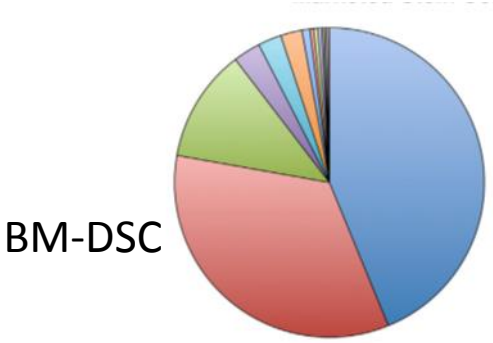
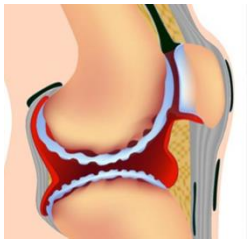
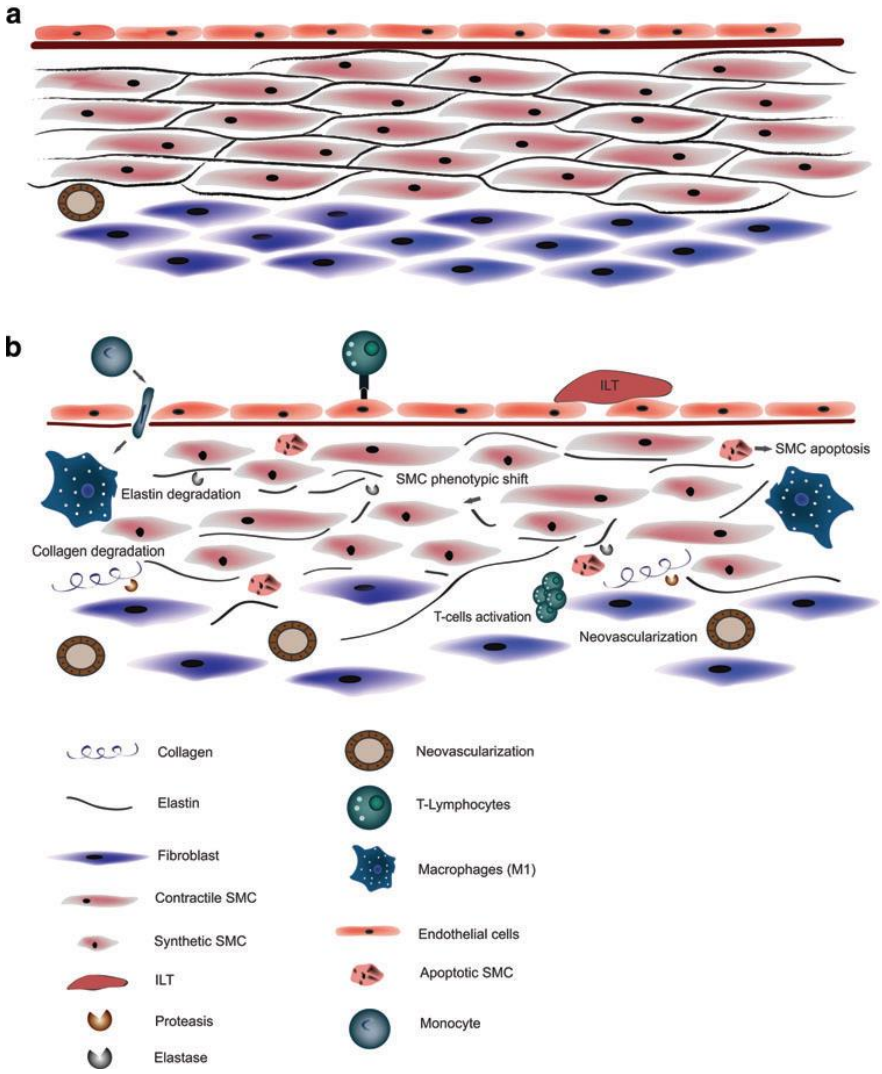


Turner L, Knoepfler P. *Selling Stem Cells in the USA: Assessing the Direct-to-Consumer Industry.*

Cell Stem Cell 2016; 19:154



Parvizi M, Harmsen MC. Therapeutic Prospect of Adipose-Derived Stromal Cells for the Treatment of Abdominal Aortic Aneurysm. Stem Cells Dev. 2015 Jul 1;24(13):1493-505.



Normal Artery

Vascular endothelial cells

Connective tissue layer

Elastic lamina

Aneurysm

Adhesion of inflammatory cells

Collagen degradation

Elastin degradation

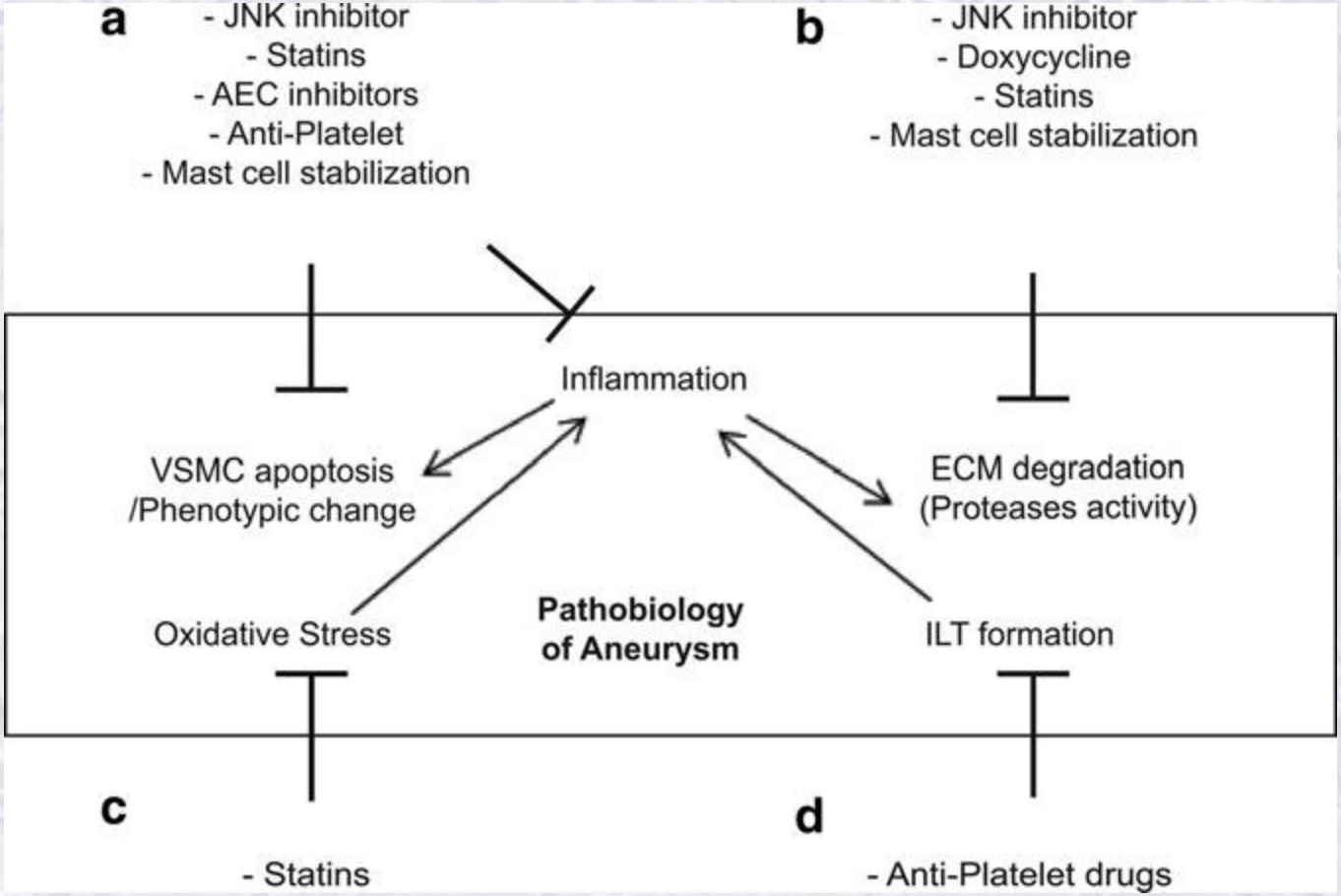
SMC apoptosis

T cell infiltration

Neovascularization

Suppression of inflammation; Rescue of SMCs from apoptosis;

Elevated production of ECM components



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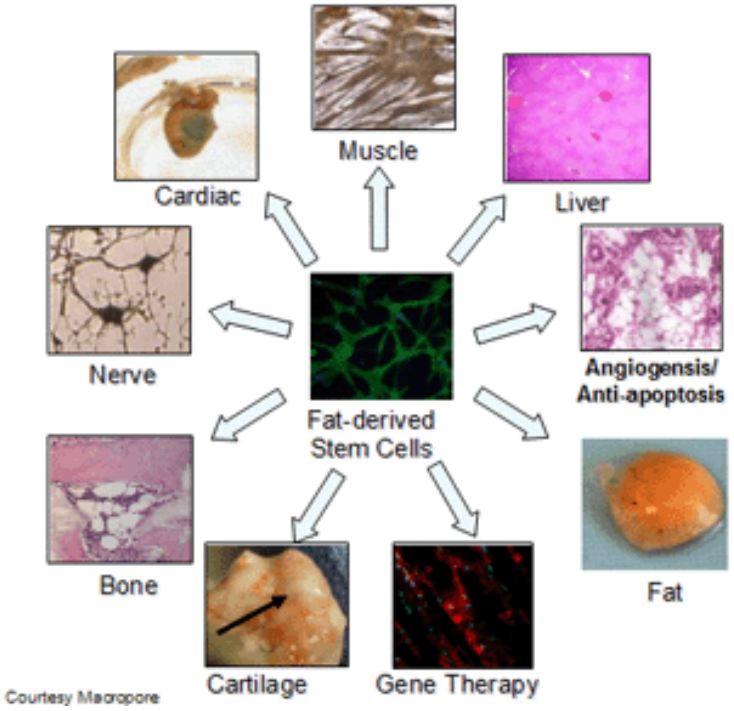
Adipose-derived stem (stromal) cells (ADSC)

- Easily available and pluripotent
- Expansion to obtain high cell numbers *in vitro*
- Differentiation into osteoblasts, adipocytes, chondrocytes, endothelial cells and smooth muscle cells (SMC)
- Resident in target tissue for prolonged times
- Release of FGFs, IGFs, VEGF, HGF, IL-8, MCP-1, IDO, PGE-2
- Synthesis of ECM components: collagen, fibronectin, elastin
- Proangiogenic, antiapoptotic, antiinflammatory role
- Remodeling of AAA in experimental models
- Immunomodulation of inflammation

ADSC - Pluripotency



Source: VETstem Biopharma

Cellular therapeutic effect?
Secreted mediators?

Fat – Liposuction

Special/Conventional Equipment

Simple explant culture

Collagenase/Purification

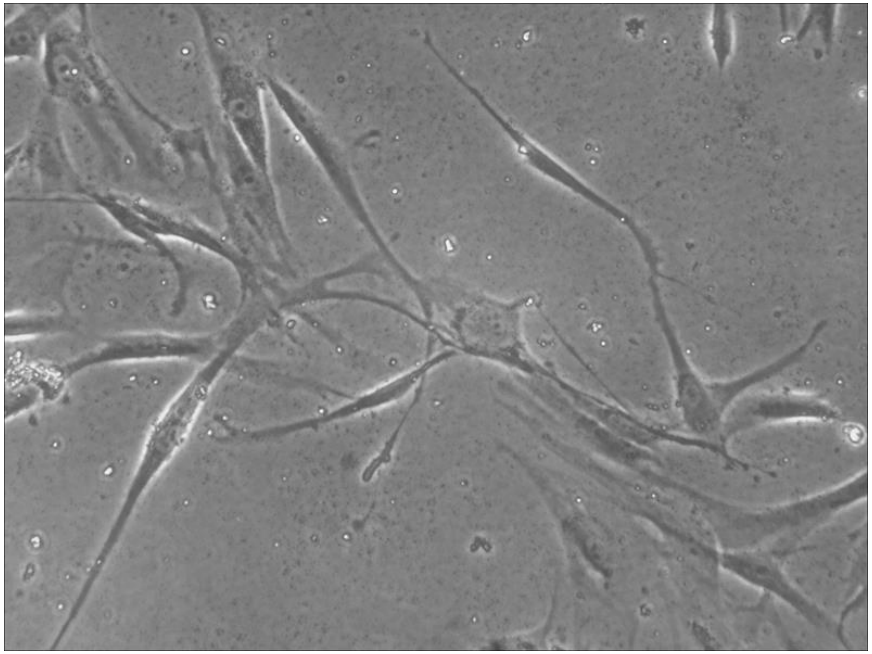
Quality control (CD markers)

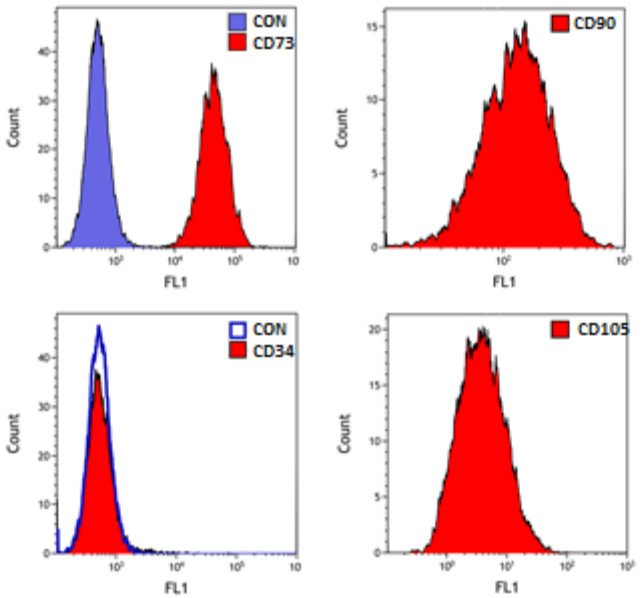
<u>Legal situation</u>:

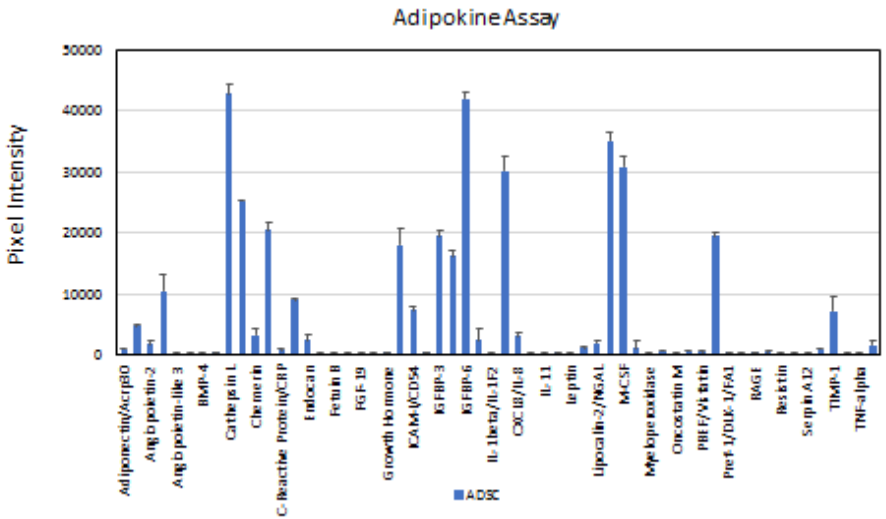
„Hospital Exemption“ for autologous

Advanced Therapy Medicinal Products

ADSC







CD73: 5'-Nucleotidase Ecto
CD90: Thy-1
CD105: Endoglin

CD34: Hematopoietic progenitor cell antigen

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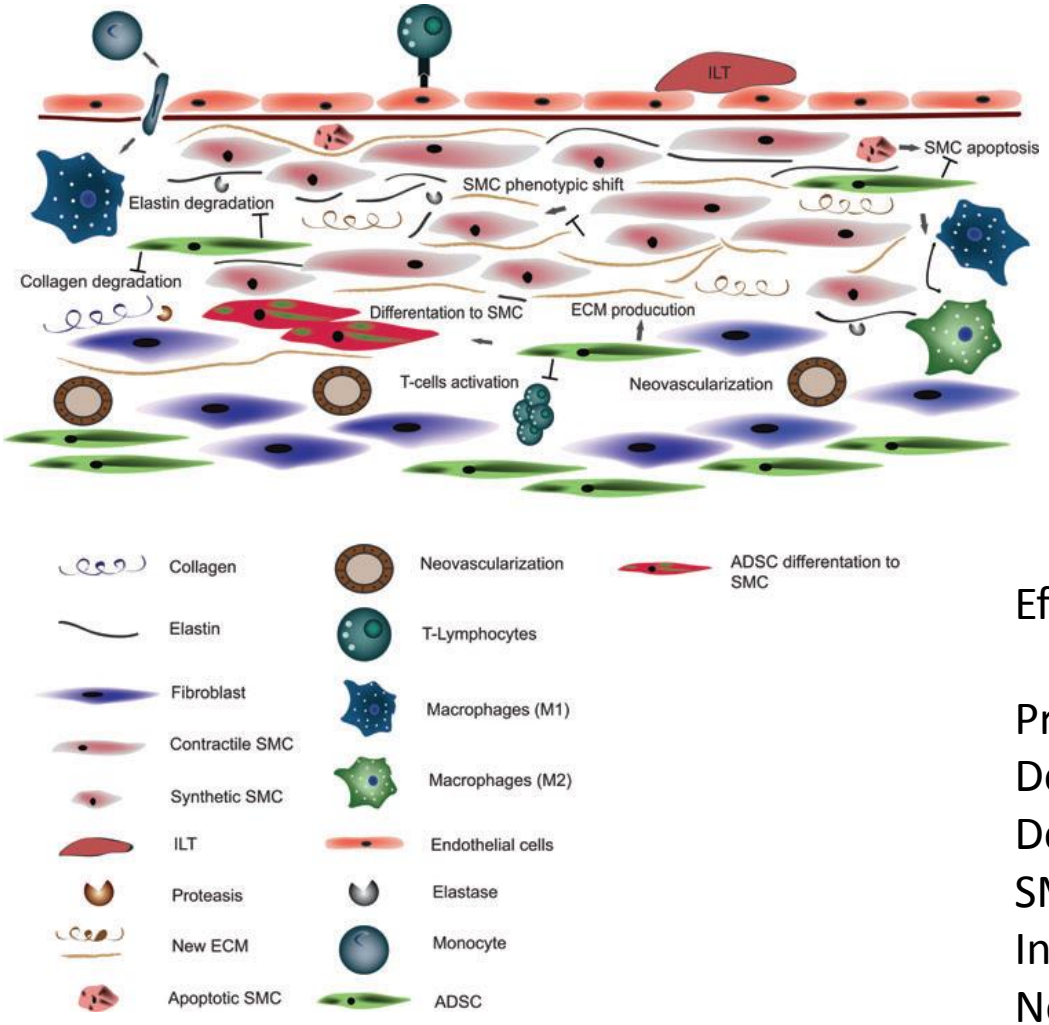

Potential normalization of an aneurysm in presence of ADSCs

Effects of ADSCs:

Preservation of elastin
Decreased inflammation
Decreased proteolysis
SMC survival
Increased ECM production
Neovascularization

Experimental Animal Models

Different AAA models: xenografts, Ang-II infusion, elastase-induction,…

Intravenous, endovascular, endoluminally administration

Vascular smooth muscle cells; BM-MSC; ADSC

- **AAA formation prevented, decreased infiltration and proteolysis**
- **Aneurysm diameter stabilization**
- **Aortic diameter and elastin stabilization, decreased MMP**
- **Decreased AAA diameter, decreased infiltration**
- **Lower inflammation**
- **Decreased diameter expansion, formation of SMC^+ tissue**
- **Decreased AAA diameter, elastin content preserved**
- **Decreased aneurysm formation, MMPs decreased**
- **Inhibition MMP-2, reconstruction of elastin fibres**

Stem cell therapy for aneurysm ?

- Stem cells available +
- Save culture conditions +
- Route of administration?
- Good retention in target tissue?
- Biomaterials for delivery?
- Direct effect vs. paracrine signaling?
- Perivascular administration more effective?
- Study of appropriate animal models.