

İleri Hücre Biyolojisi

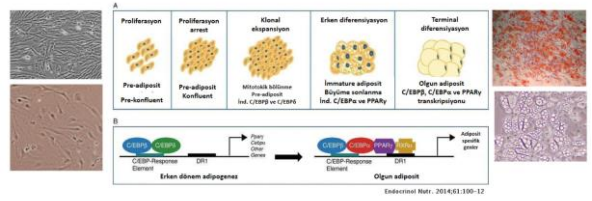
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Öğr. Gör. Dr. Mahmut PARMAKSIZ

Ankara Üniversitesi Kök Hücre Enstitüsü

Yetişkin Kök Hücreleri

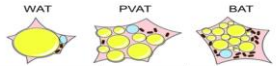
Adipoz Doku Kök Hücreleri



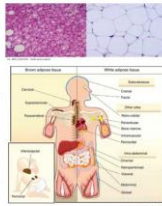
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Yetişkin Kök Hücreleri

Adipoz Doku Kök Hücreleri



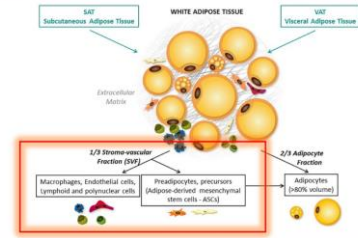
	Beyaz (WAT)	Perivasküler (PVAT)	Kahverengi (BAT)
Lipit içeriği	Çok yüksek, tek damla	Yüksek, çok damla	Yüksek, çok damla
Mitokondrial içerik	Çok düşük	Yüksek	Çok yüksek
UCP1 ekspresyonu	Çok düşük	Lokasyona bağlı	Yüksek
Vaskülerizasyon	Yeterli,	Adventitia teması	Yüksek perfüzye
Fonksiyon	Lipit depolama, endokrin fonksiyon	Thermogenez, vasküler ton	Thermogenez
Lokasyon	Subkutan veya intra-abdominal	Damar çevresi	İnter ve sub-skapular



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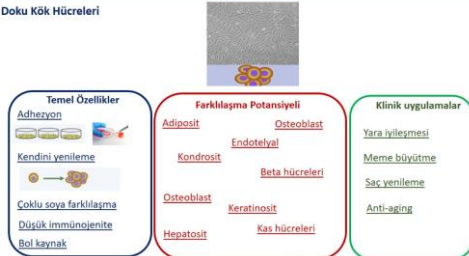
Adipoz Doku Kök Hücreleri



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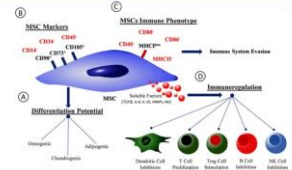
Mezodermal: Adipositler, fibroblastlar, myositler, osteositler, kondrositler vb.
Non-mezodermal: Endotelial, nöral-benzeri hücreler, pankreatik islet hücreleri, hepatositler vb.

Çözünür Faktörler

Adiponectin, angiotensin, cathepsin D, penetraxin, pregnancy zone protein, retinol binding protein, CXCL12, HGF, GM-CSF, ILs 6, 7, 8, 11, TNF-α, VEGF, BDNF, NGF, GDNF, IGF-1, TGF-β, FGF-2, PGE2,

İmmünomodülatör

Allojenik kullanım potansiyeli
 MLR tepki baskılama,
 PHA-stimulated lenfosit proliferasyon inhibisyonu



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İmmünofenotipik tanımlama

TABLE 1. Potential surface markers for the identification of ADSCs.

Surface marker	Name	Category	Positive/negative
CD11b	α_4 integrin	Adhesion molecule	Negative
CD104	β_1 integrin	Adhesion molecule	Negative
CD114	Lipopolysaccharide	Receptor molecule	Negative
CD342	Leukocyte common antigen	Receptor molecule	Negative
CD39	MB-1	Receptor molecule	Negative
CD116	Fc receptor	Receptor molecule	Negative
HLA-DR	Human leukocyte antigen DR	Histo-compatibility antigen	Negative
CD73	Ecto-5' nucleotidase	Surface enzyme	Positive
CD13	Aminocephalase	Surface enzyme	Positive
CD10	Endopeptidase	Surface enzyme	Positive
CD105	Endoglin	Adhesion molecule	Positive
CD49d	α_4 integrin	Adhesion molecule	Positive
CD329	β_1 integrin	Adhesion molecule	Positive
CD44	Hyaluronate	Receptor molecule	Positive
CD146	Thrombospondin	Receptor molecule	Positive
CD117	c-kit	Receptor molecule	Positive
CD90	Thy-1	Extracellular matrix	Positive
CD146	Slac-18	Extracellular matrix	Positive
CD34	Hemopoietic progenitor cell antigen	Stem cell	Positive
CD133	Promitin-1	Stem cell	Positive

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Adipoz Doku Kök Hücreleri

ISCT : CD105, CD73, CD90
CD45, CD34, CD14, CD11b, CD79a, CD19, ve
HLA-DR

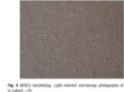


Fig. 4. ADSCs morphology (left) under microscope at passage 4 (100x).

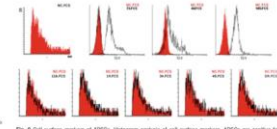
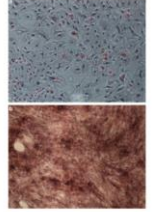


Fig. 8. Cell surface markers of ADSCs. Histogram analysis of cell surface markers. ADSCs are positive for CD73, CD34, and CD105, and negative for CD19, CD34, CD45, and HLA-DR.



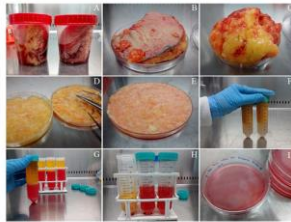
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Yetişkin Kök Hücreleri

Adipoz Doku Kök Hücreleri

İzolasyon

- Atık yağ dokusu
- Seri yıkama-kan uzaklaştırma
- Damarların temizlenmesi
- Enzimatik degradesyon
- Santrifüjleme
- Yüzey adaptasyonu



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Yetişkin Kök Hücreleri

Adipoz Doku Kök Hücreleri



FIGURE 1: The typical process for the preparation of ADSCs from human adipose tissue. SVF: stromal vascular fraction.

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Adipoz Doku Kök Hücreleri

Alternatif Yaklaşım – ADMSCs vs SVF



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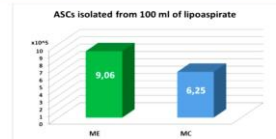
Yetişkin Kök Hücreleri

Adipoz Doku Kök Hücreleri

CD31(-), CD34(+), CD45 (-), CD73(+) ve CD90(+)

Mekanik + Enzimatik : $9,06 \times 10^5$ (ADMSCs) / 100 mL adipoz doku
($3,5 \times 10^7$ toplam hücreden %25,9 verim) (80 dk)

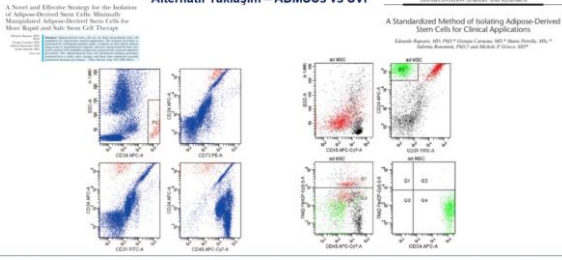
Mekanik : $6,25 \times 10^5$ (ADMSCs) / 100 mL adipoz doku
($1,25 \times 10^7$ toplam hücreden %5 verim) (15 dk)



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Yetişkin Kök Hücreleri

Alternatif Yaklaşım – ADMSCs vs SVF



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Yetişkin Kök Hücreleri

Table 1. Flow of care devices for best site separation of SVF

Medical device	Manufacturer	Closed semi-closed	Separation method	Preceded fat quantity (g)	Process duration (min)	Cell yield of fat Device/control (D/C)	Cell viability (%) or D/C
Celtrion B-800/350	Cytori Therapeutics, South Korea	Closed	Enzymatic	300g	90	2.41 × 10 ⁷ NP	NP
900000	Intellusys Inc.	Closed	Enzymatic	300g	90	0.425 × 10 ⁷ ± 0.047 × 10 ⁷ 0.795 × 10 ⁷ ± 0.228 × 10 ⁷	50-84% 15.4
QCS SVF-1	QCS Group Inc.	Closed	Enzymatic	300g	90	0.25-2.0 × 10 ⁷	64.2 ± 15.4
Xceltra™	Tissue Genesis, Inc.	Closed	Enzymatic	60	90	0.25-2.0 × 10 ⁷	64.2 ± 15.4
Puregra™	Eurokatione	Semi-closed	Mechanical	250	190	0.25 × 10 ⁷ ± 0.037 × 10 ⁷ 0.228 × 10 ⁷	77%
Semgra™	Procell	Closed	Mechanical	200	110	0.255 × 10 ⁷ ± 0.220 × 10 ⁷ 0.276 × 10 ⁷ ± 0.228 × 10 ⁷	69%
Chelator™	PRC International Co., Ltd.	Semi-closed	Mechanical	200	90	0.05 × 10 ⁷	NA
Sepax™	Epocale Corp SA	Semi-closed	Mechanical	300	90-120	2.8 ± 1.2 × 10 ⁷ ML	NA
LINEASTAR™	NeoGenex	Closed	Not specified	NP	NP	1.1 × 10 ⁷ ± 1.1 × 10 ⁷ 2.2 × 10 ⁷ ± 1.7 × 10 ⁷	NA
Lipote Maxion™	Medi-Khan™	Semi-closed	Enzymatic	NP	88-120	0.15 × 10 ⁷	50-84

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Manüplasyon içermeyen uygulamalarda kısıtlamalar uygulanmaz.

[Regulation (EC) No 1394/2007 of the European Parliament and of the Council].

Yetişkin Kök Hücreleri

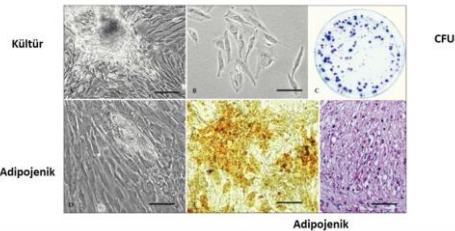
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Farklılaşma	Kullanılan ajanlar
Adipojenik	Insulin; isobutylmethylxanthine (IBMX); dexamethasone; rosiglitazone; indomethacin.
Osteojenik	Dexamethasone; β-glycerophosphate; vitamin D3; bone morphogenetic protein (BMP-2)
Kondrojenik	insulin growth factor (IGF); BMPs; transforming growth factor-β (TGF-β)
Miyojenik/kardiyomyojenik	Dexamethasone; hydrocortisone; IL-3; IL-6
Nörojenik	Valproic acid; epidermal growth factor (EGF); fibroblast growth factor (FGF); nerve growth factor (NGF) and brain-derived neurotrophic factor (BDNF)
Tendinous	FGF; platelet derived growth factor (PDGF-BB); EGF; TGF-β; IGF-1; BMPs

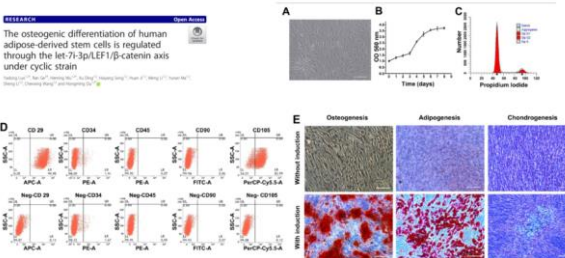
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