

Nedir Bu Kk Hcre ?



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KAYSERİ 2013-2014

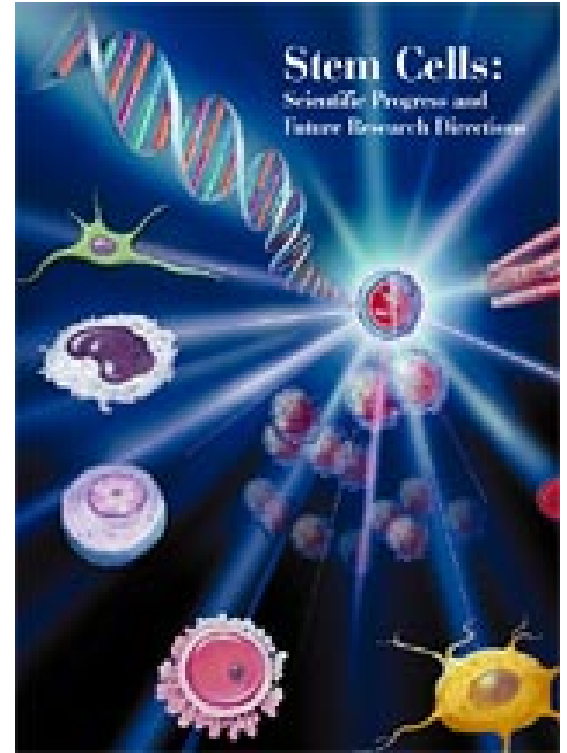
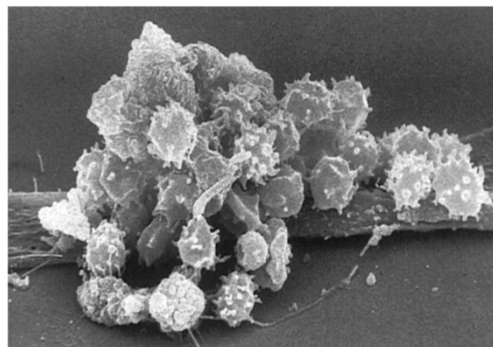
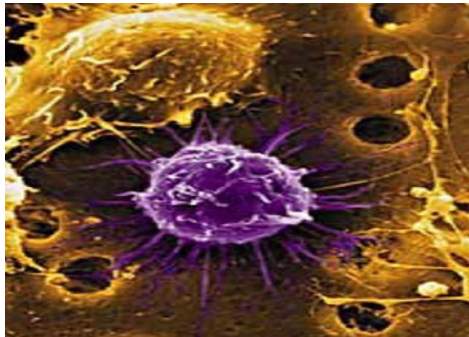
Gündem

- Kök hücre “Stem Cell” nedir?
- Kök Hücre Gelişim Basamakları...
- Kök hücre çeşitleri
- Embriyogenezin Evreleri
- İnvitro Embryonik Kök Hücre Dizilerinin Oluşumu
- Kök hücre yüzey işaretçileri
- Embriyonik kök hücre
- Ergin kök hücre
- Kök Hücre ile tedavi edilen hastalıklar
- Hematopoetik Kök Hücre Nakli

Kök hücre “Stem Cell” nedir?

Sonsuz bölünme ve farklılaşma yeteneğine sahip tek hücreli genomik yapıdan fenotipik olarak farklı hücrelere dönüşebilen hücrelerden oluşur.

- Self Renewal: Devamlı bölünürken, kendi yedeğini verebilmesi
- Pluripotent: Farklı hücrelere gelişebilme ve değişebilme (differansiasyon) yeteneği (potency)



Kök Hücre Gelişim Basamakları...

- Totipotent kök hücre
- Pluripotent kök hücre
- Multipotent kök hücre
- Unipotent kök hücre

Hemostasis ve doku replasmanından sorumlu

Kök hücre çeşitleri

Tanımlar

Her bir hücre yeni bir bireyi geliştirebilir.

Her bir hücre 200'den fazla somatik hücreye dönüşebilir.

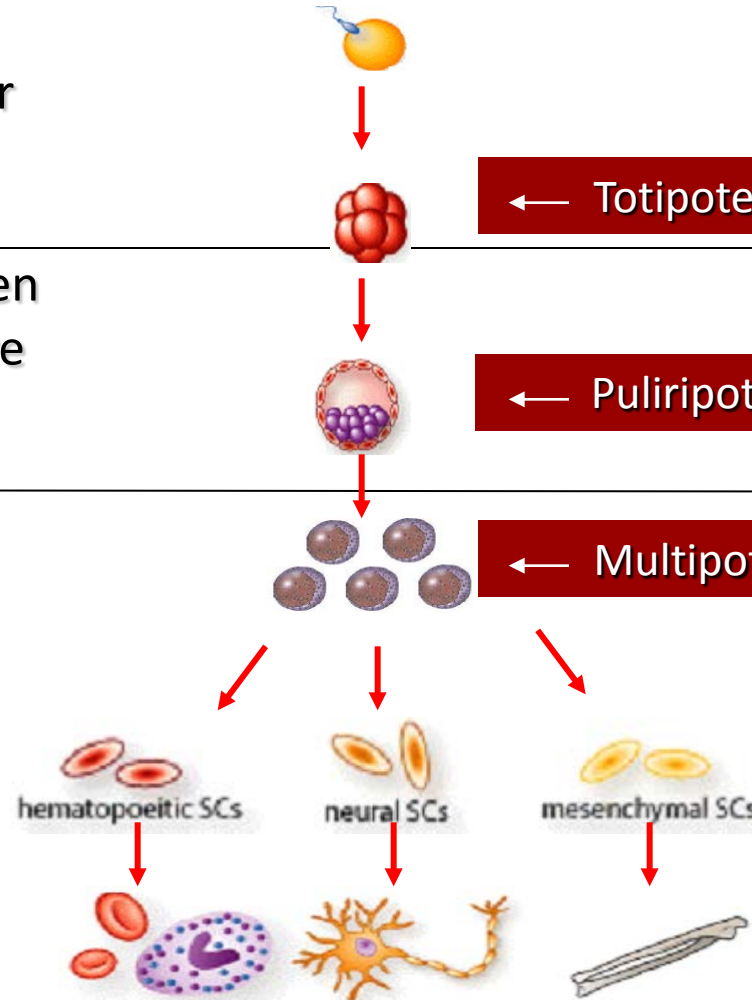
Plastisite kabiliyeti korunmuştur, maturasyon eğilimli

Örnekler

Erken Embriyonik hücreler (1-3 günlük)

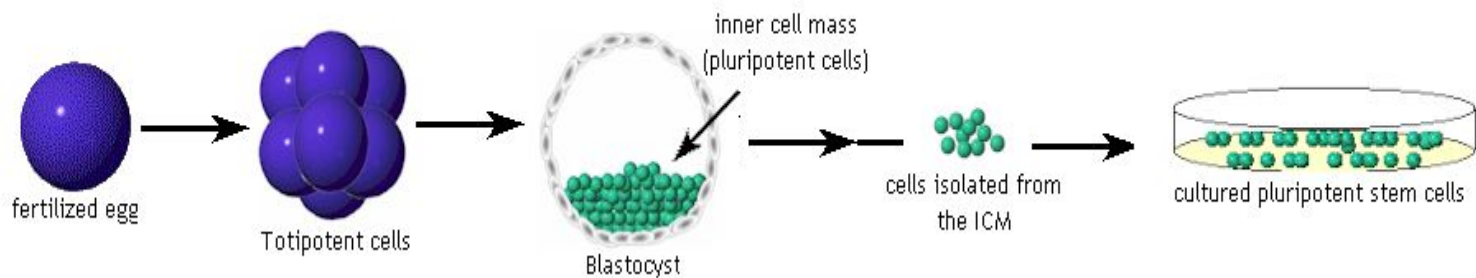
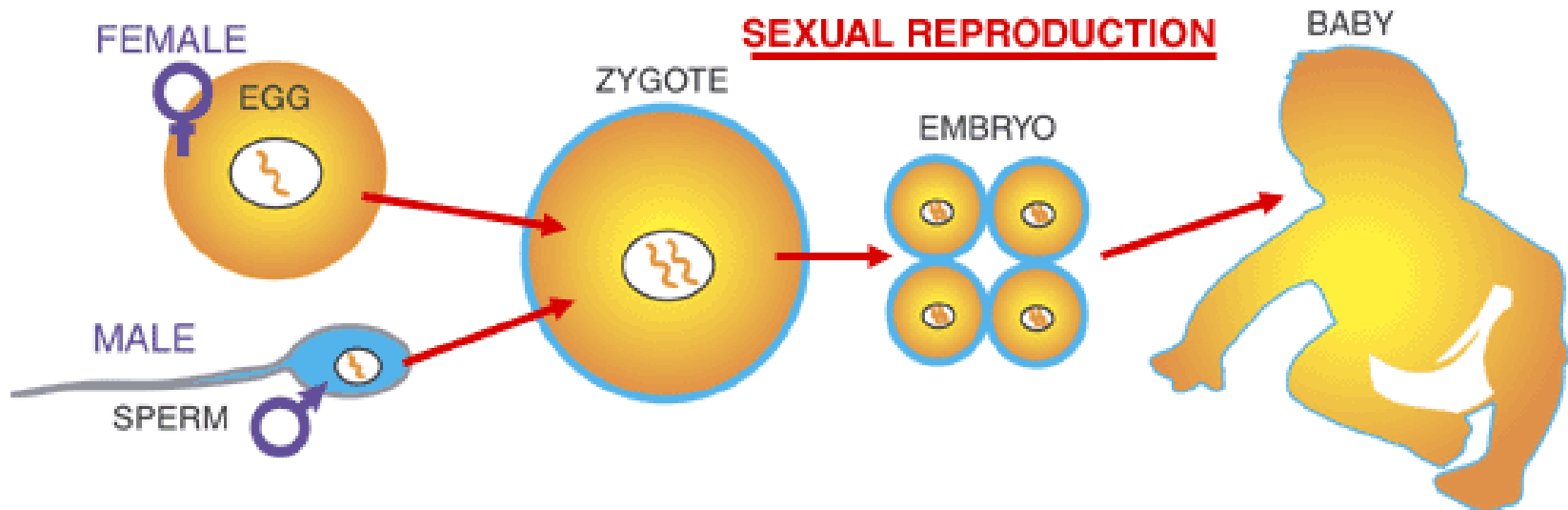
Blastosit hücreleri (5-14 günlük)

Adult kök hc Kord kanı Fetal doku

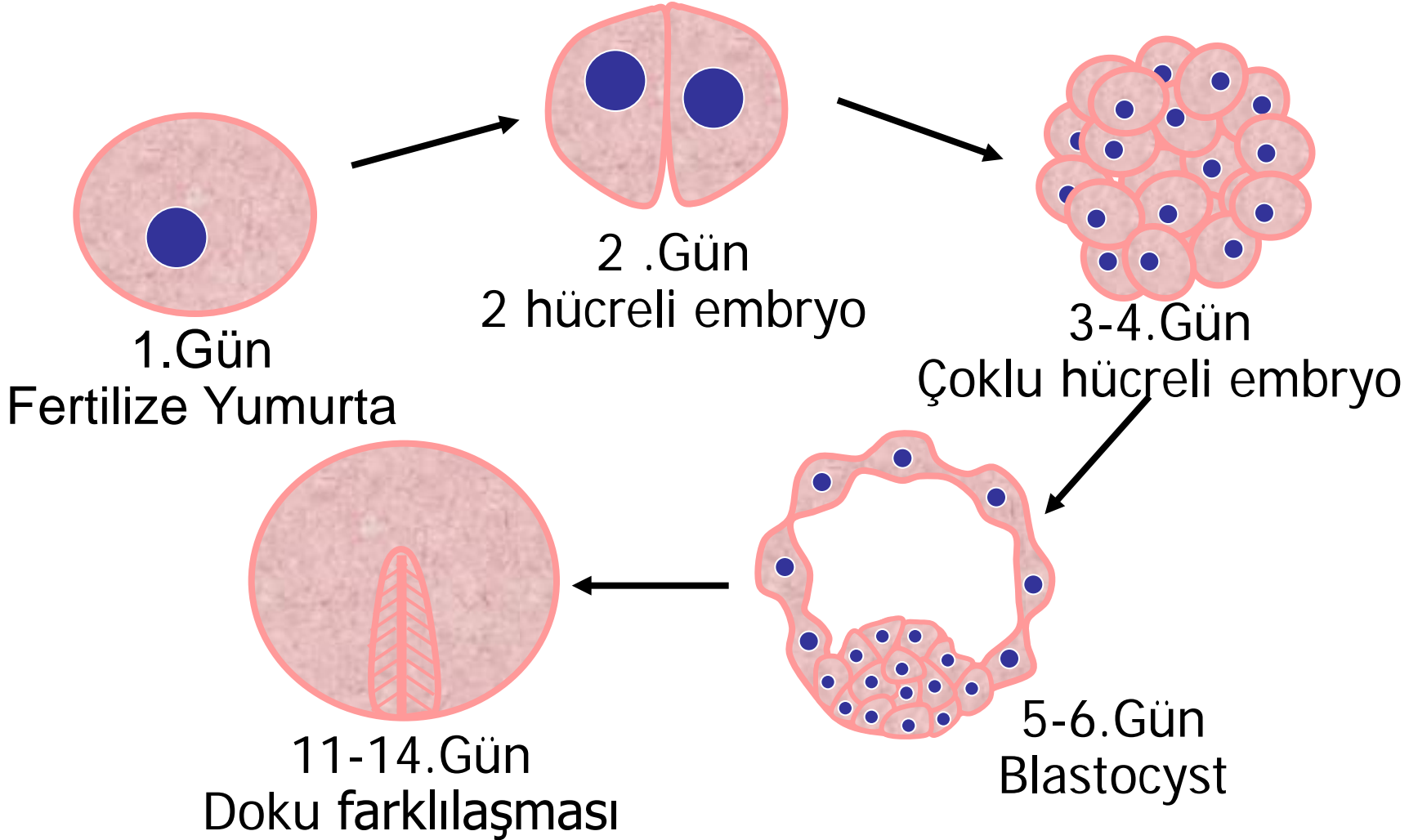


Doku hemaostasis ve Tamir [Repair]

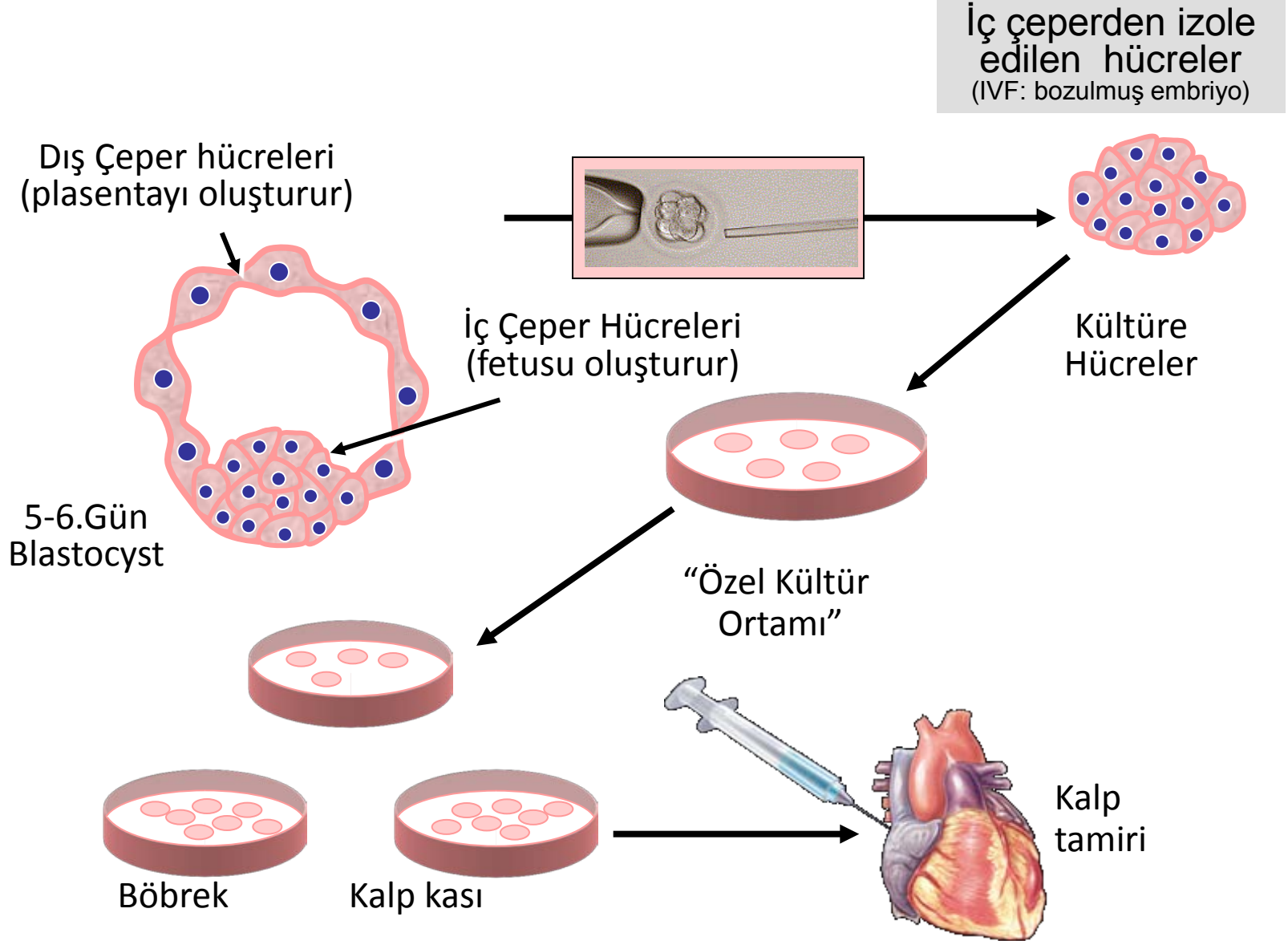
Hücreden insana.....



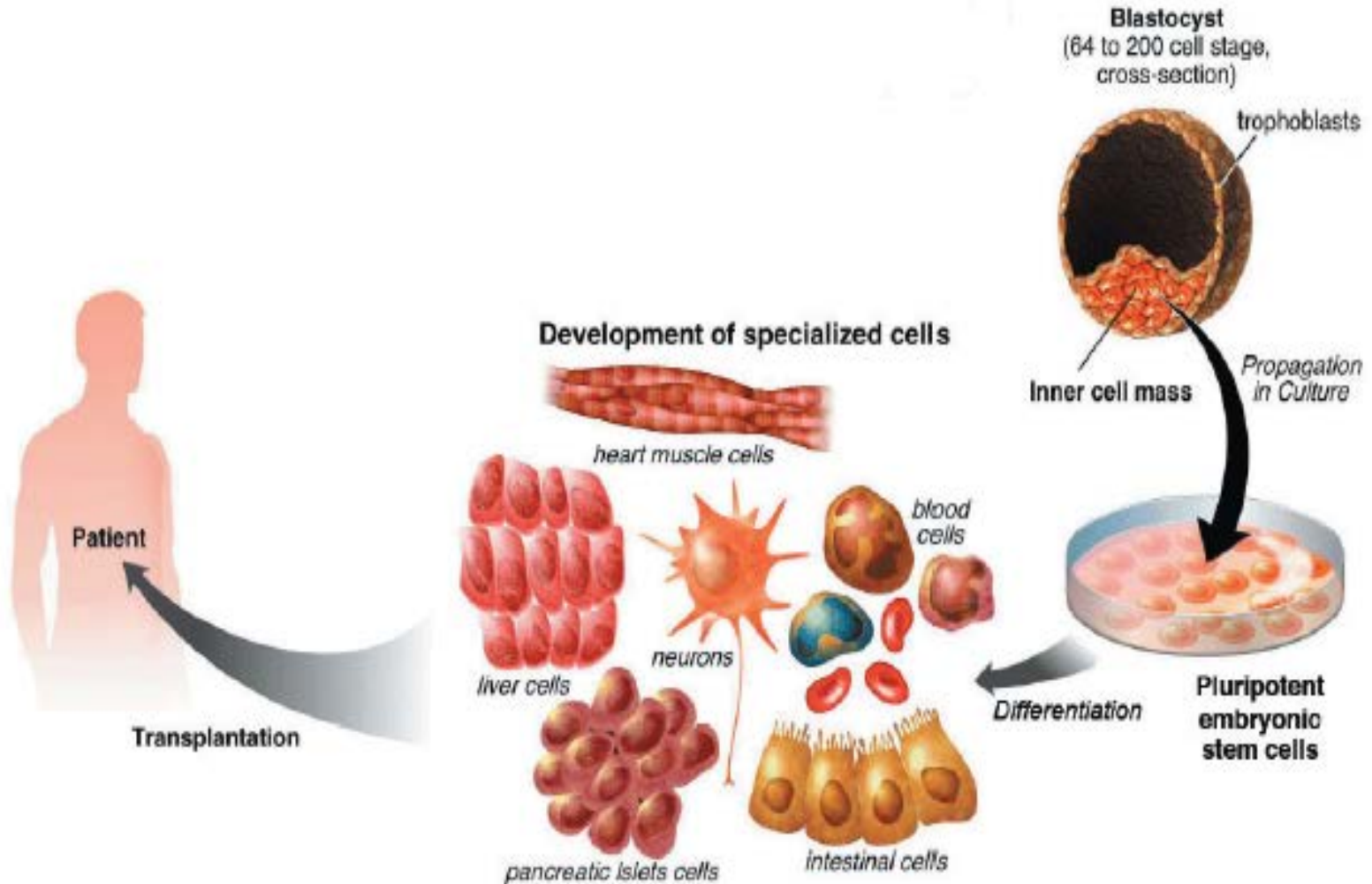
Embriyogenezin Evreleri



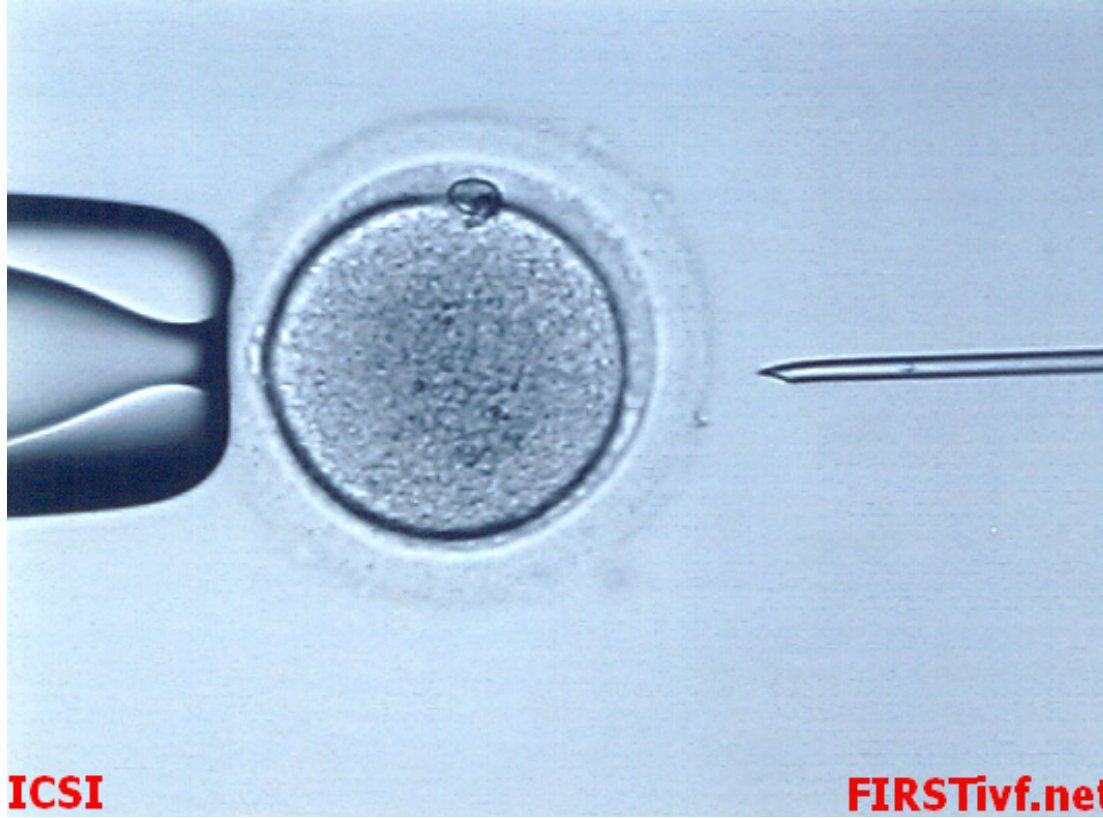
Embryonic Kök Hücre Dizileri; Oluşumu ve kullanılması



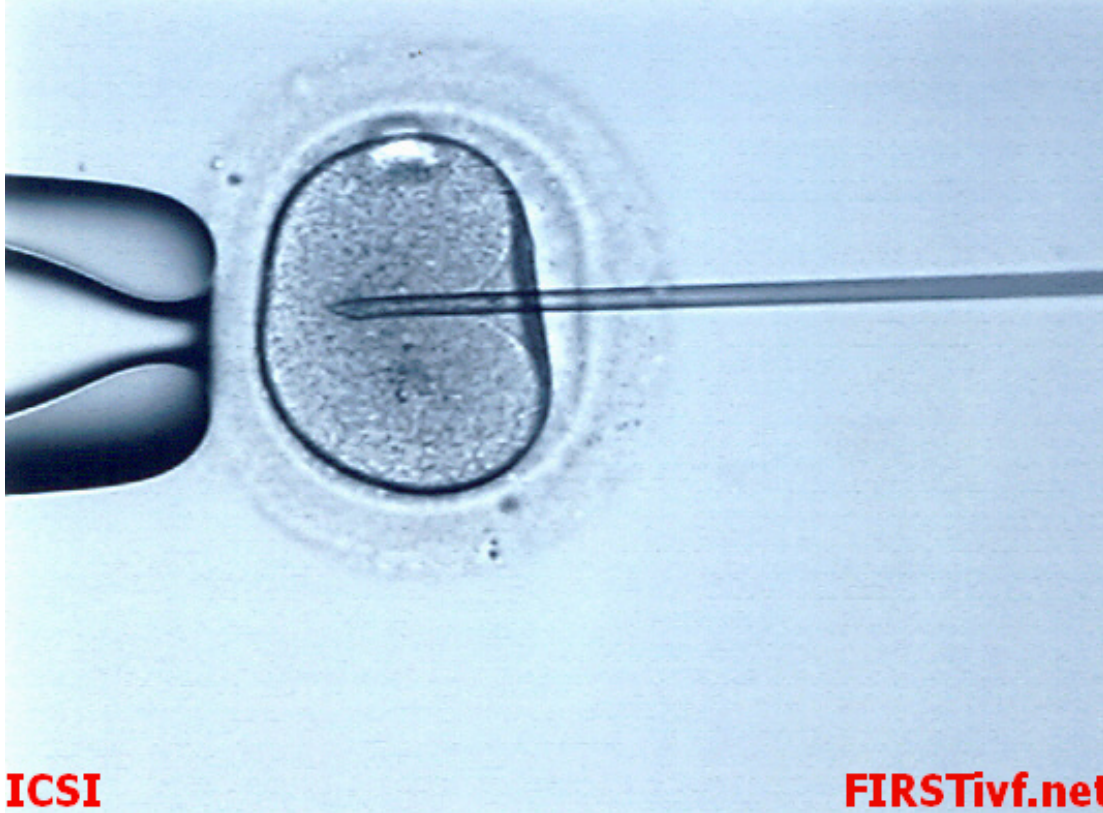
İnvitro Embryonik Kök Hücre Dizilerinin Oluşumu



Intrastoplazmik Sperm İnjeksiyonu



Intrastoplazmik Sperm İnjeksiyonu



İntrastoplazmik Sperm İnjeksiyonu



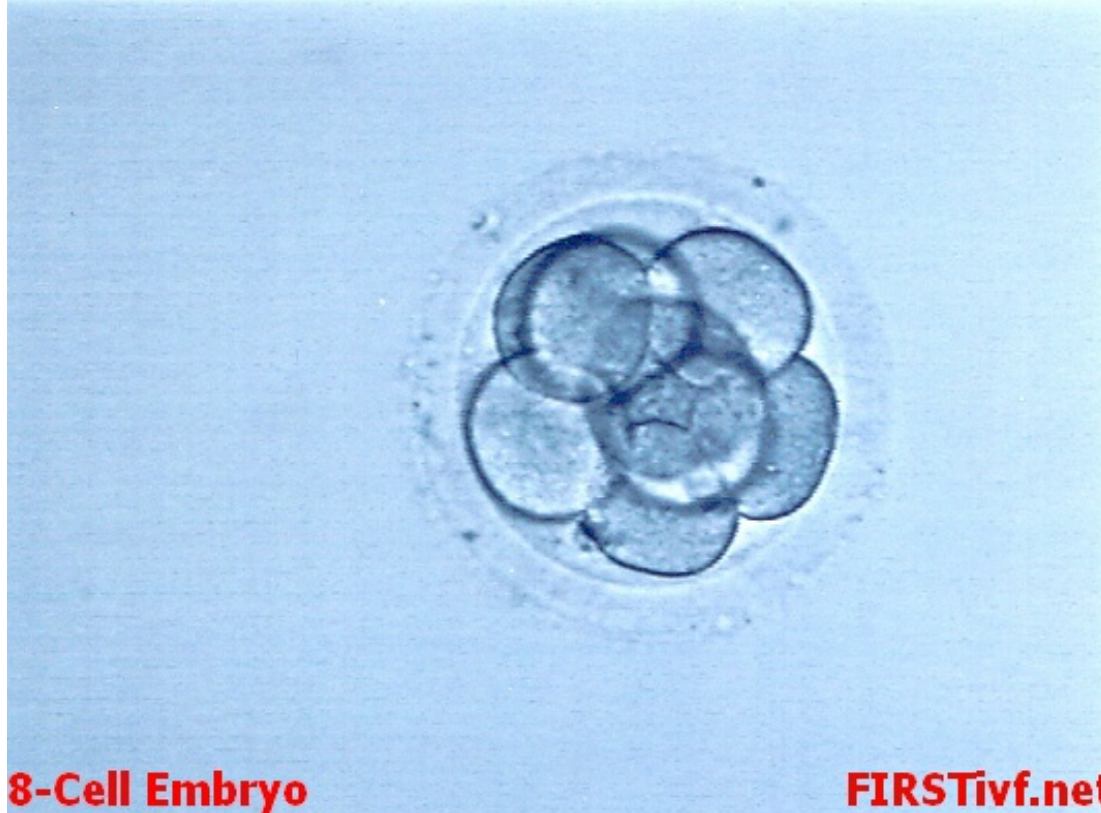
Intrastoplazmik Sperm İnjeksiyonu



İntrastoplazmik Sperm İnjeksiyonu



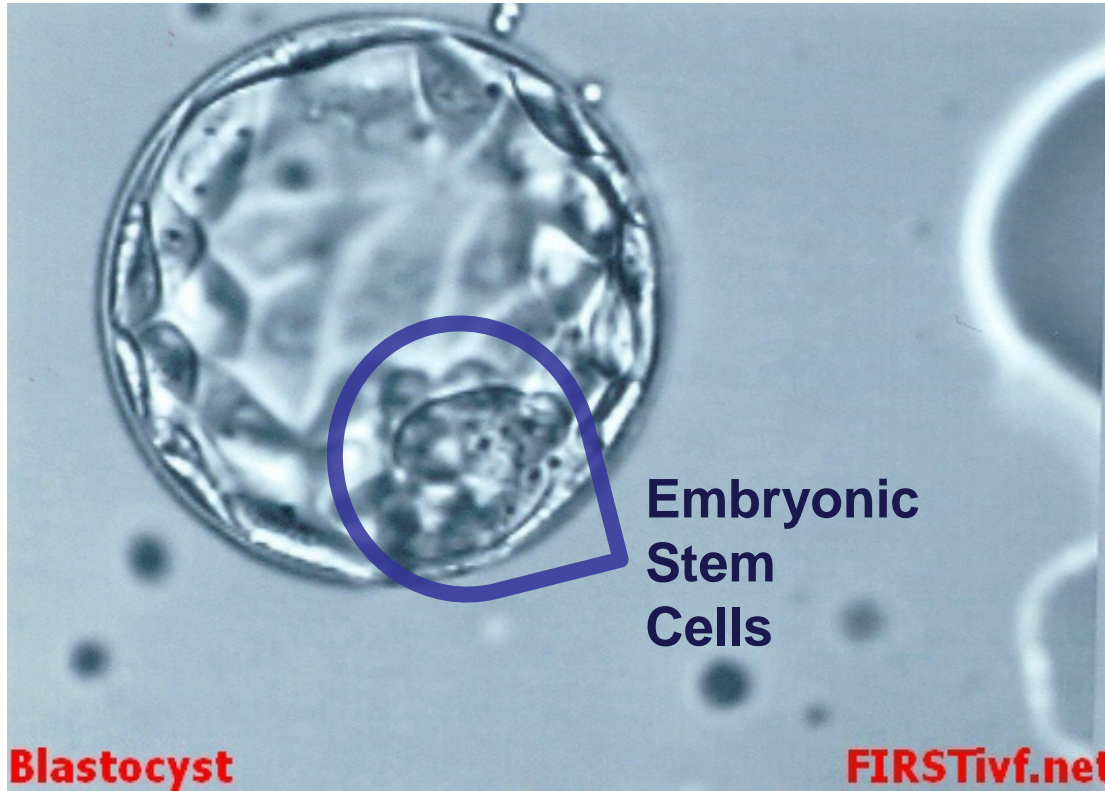
Intrastoplazmik Sperm İnjeksiyonu



İntrastoplazmik Sperm İnjeksiyonu



Intrastoplazmik Sperm İnjeksiyonu



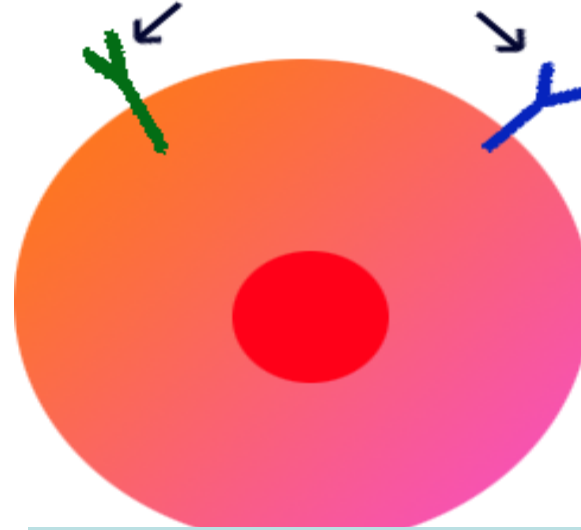
Temelde Kök hücreler

- Embriyonik kök hücre
- Ergin (adult) kök hücre

Kök Hücre Yüzey İşaretçileri

- c-Kit
- Oct4
- **CD34**
- CD38
- Cd44
- CD133
- Nestin

Yüzey işaretçileri



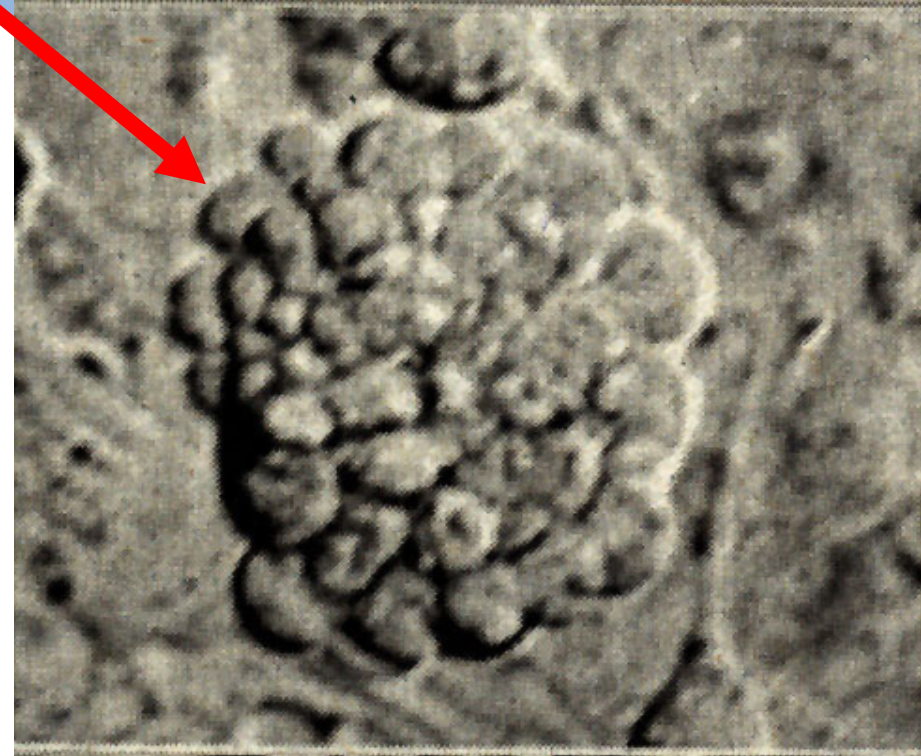
Kök Hücre

Embriyonik kök hücre

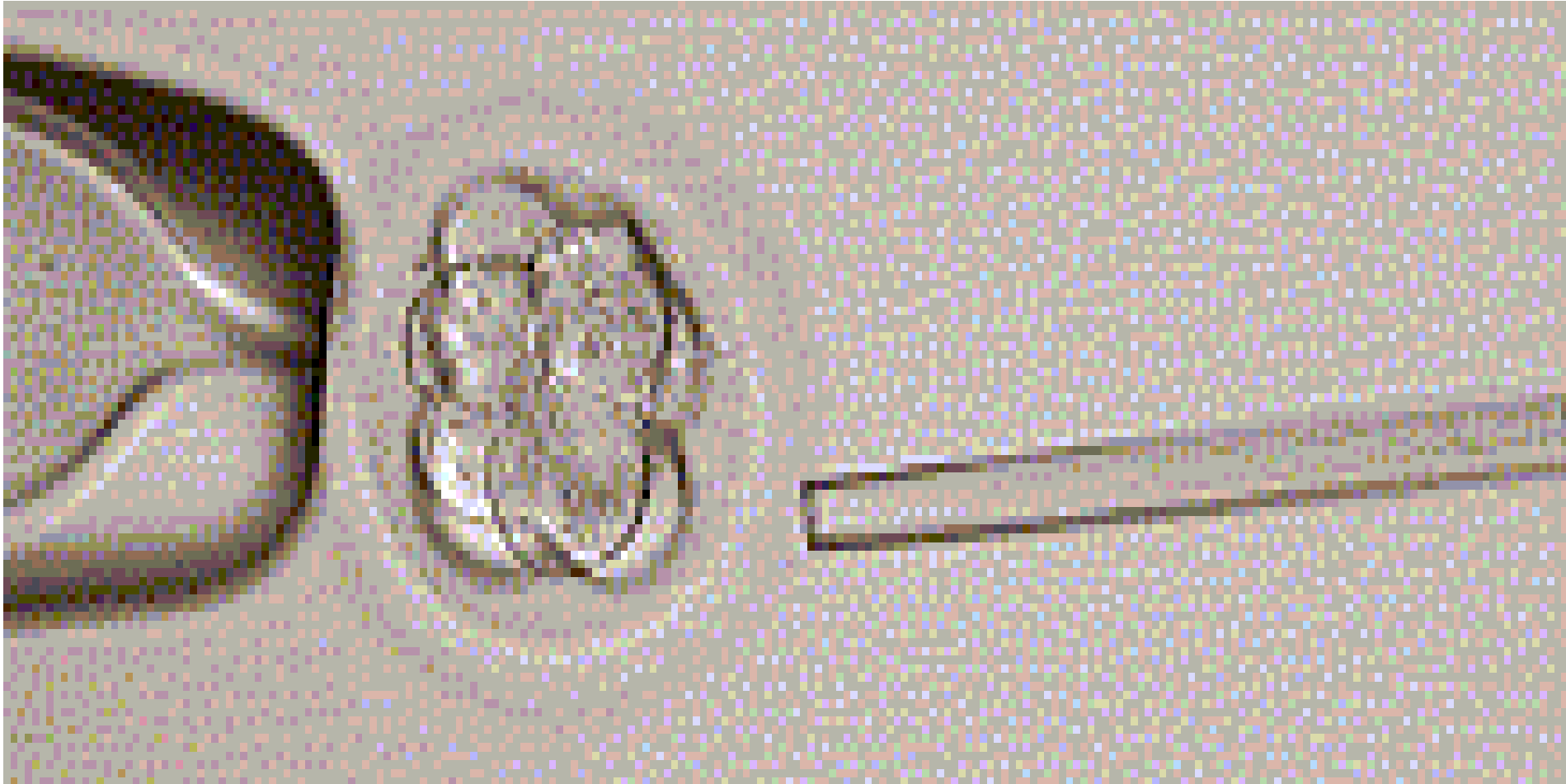
- Fertilize embriyodan elde edilir.
- “Harvest” zamanı fertilizasyonun 3-5 günü.
- “Pre-blastosist” aşaması
- Sonsuz yenilenme yeteneği vardır (totipotent).
- Tüm organizmayı ve postembriyonik doku ve organları oluşturabilme kapasitesindedir.

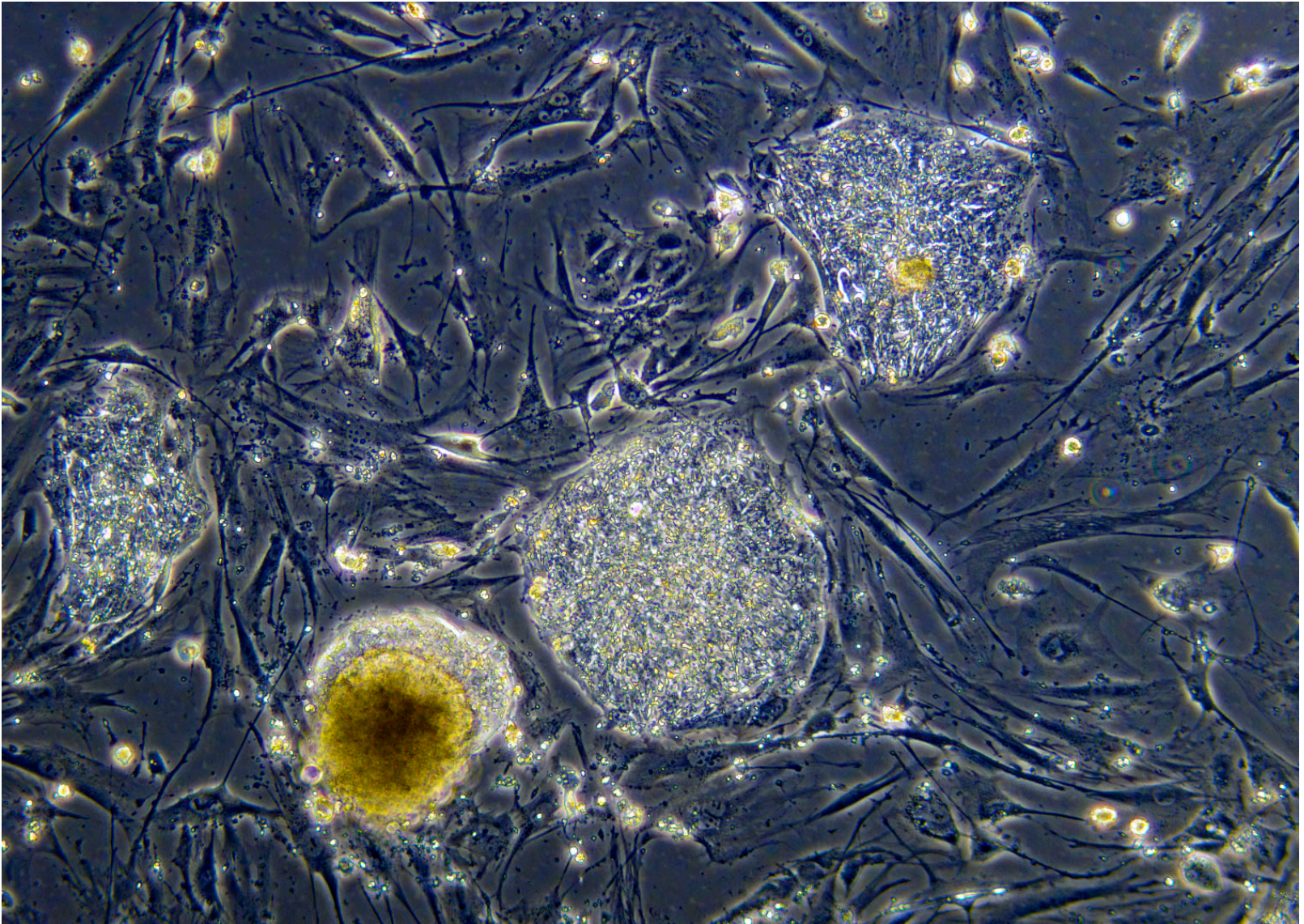


Blastosit
İç kitesinden
Embriyonik kök
Hücrelerin
İzolasyonu



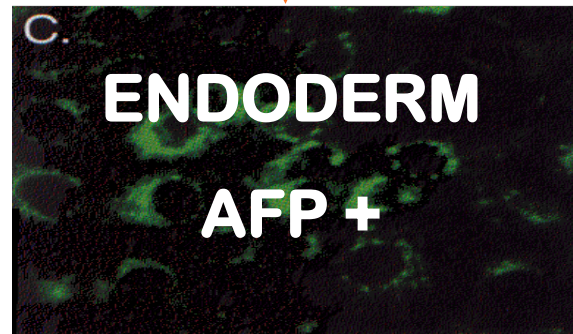
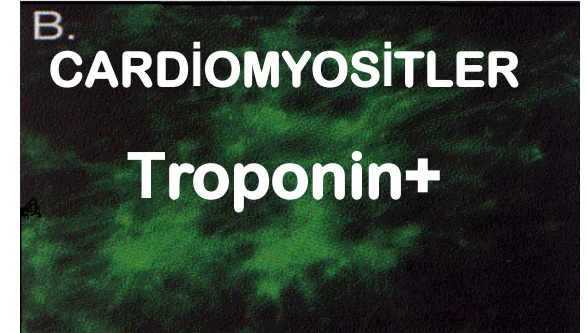
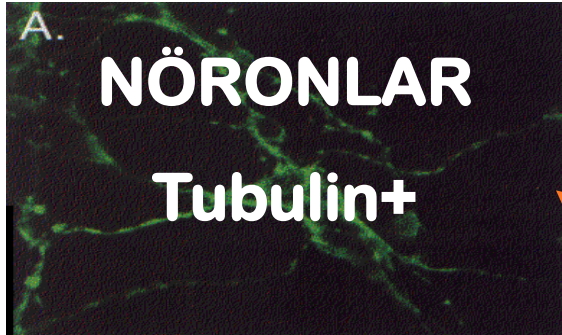
İNSAN EMBRYONİK HÜCRELERİNİN İN VİTRO KÜLTÜR İÇİN AYRIŞTIRILMASI



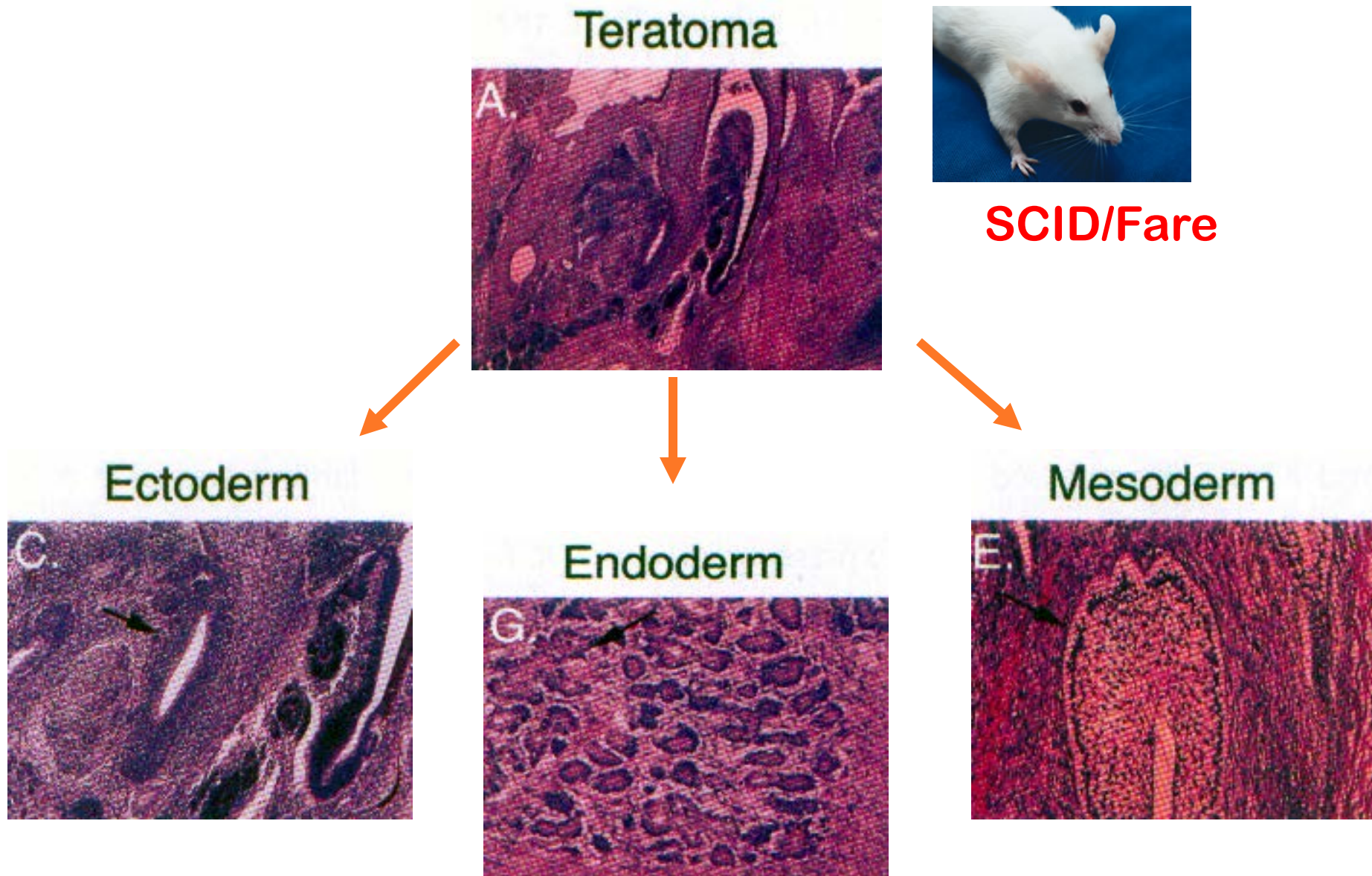


Embryonik kök hücre kolonileri

İnsan embriyonik kök hücrelerinin in-vitro farklılaşması



İnsan embriyonik kök hücrelerinin in-vivo farklılaşması

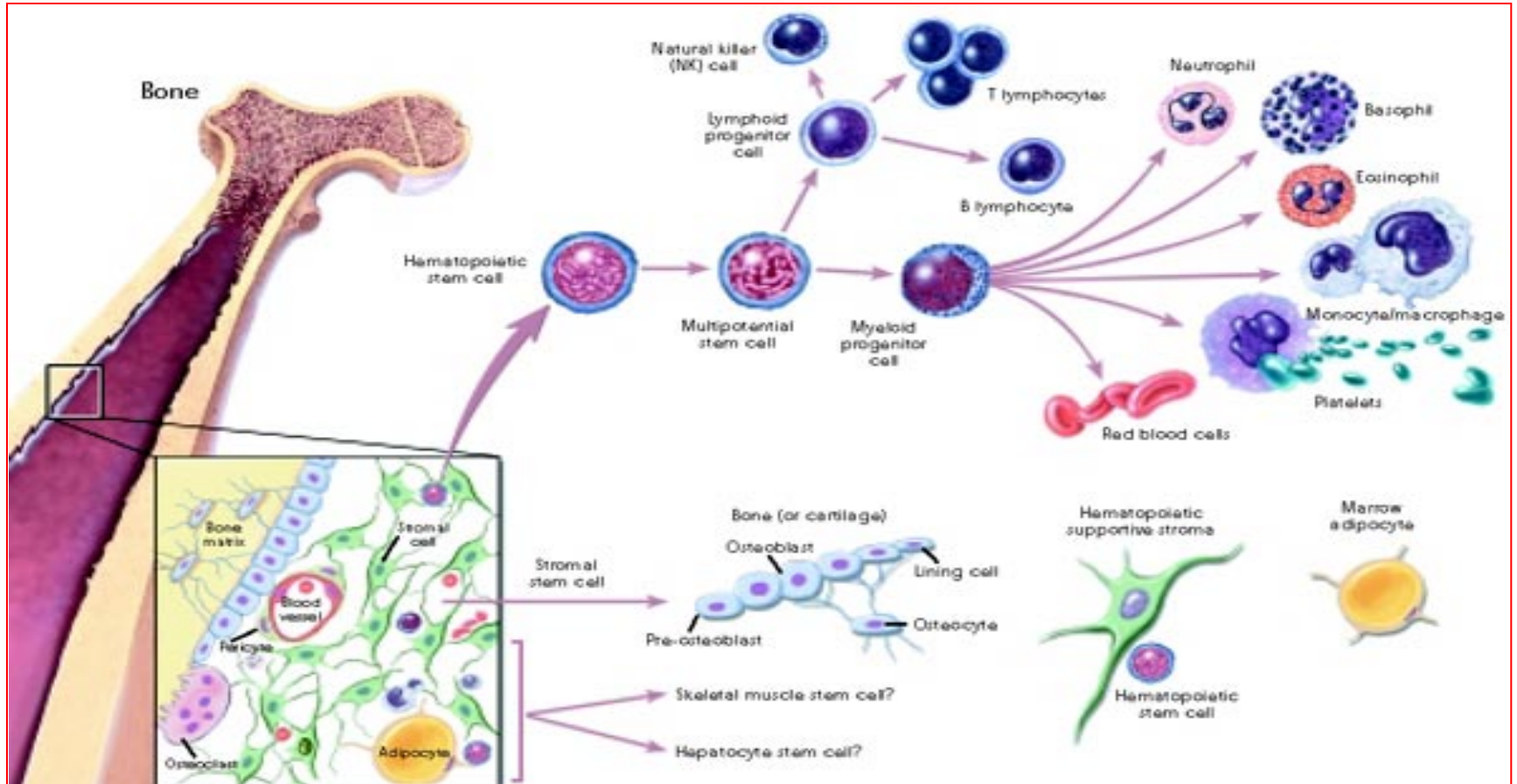


Ergin kök hücre

- Sınırlı yenilenebilme yeteneđi
- Doku replasmanı
- Puliripotent
- En iyi bilinen “ kanyapıcı kök hücre-hematopoetik stem cell” dir.
- Kaynak: kemik iliđi, Kordon kanı, plasenta ve amniyotik sıvı gibi gebelik dokuları.

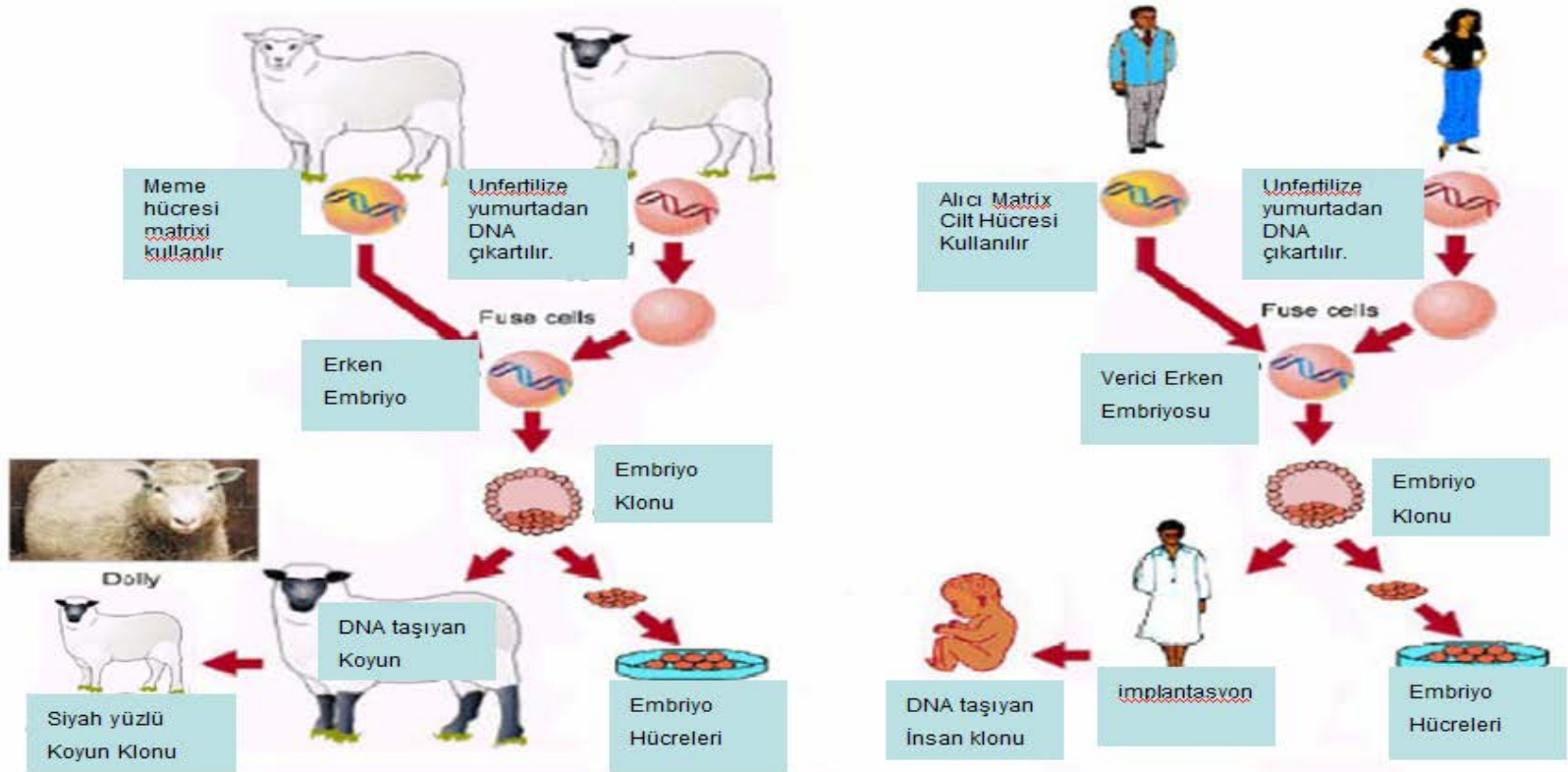
Beyin, kornea, diş pulpası, karaciger, pankreas. Deri, Kemik, kartilaj vs..... Doku replasman ve tamirinde kullanılmaktadır.

Ergin kök hücre



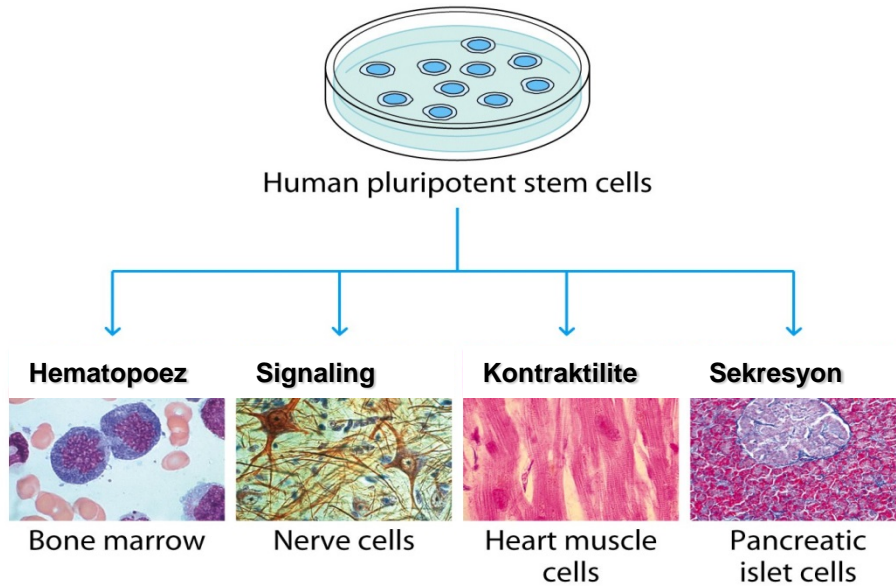
Doku Hemostasis>>>>maturasyon>>>>replasman

Ergin kök hücre <<klonlama>>



Ergin kök hücre <<Plastisite>>

- Farklı Orjin (generation)
- Farklı doku (differentiation)
- Genetik program değişikliği (genetic re-programming)

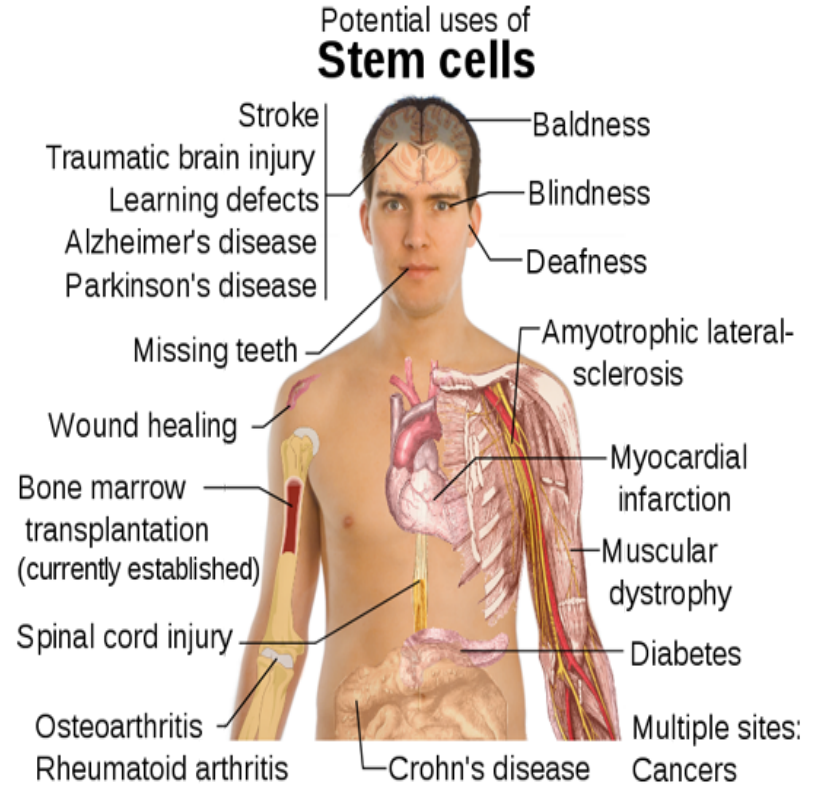
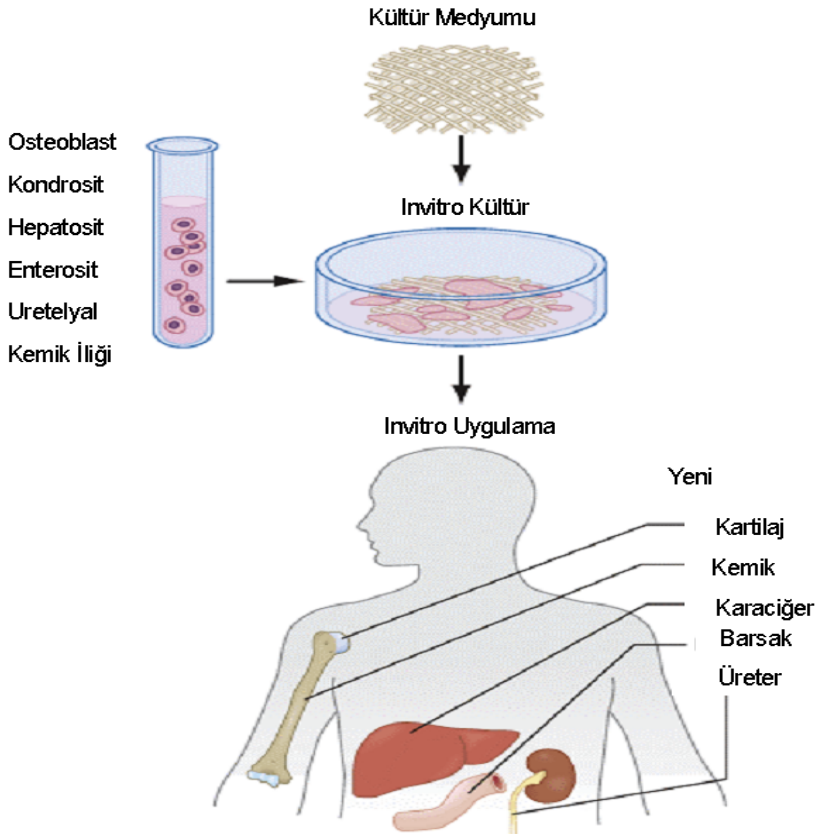


Çevresel sinyaller kök hücrelerini spesifik hücreye yönlendirmektedir.

Ergin

kök hücre

<<Kullanım>>



Kök Hücre ile tedavi edilen hastalıklar

1) Acute Leukemia	Disorders	5) Inherited Metabolic Disorders	7) Inherited Immune System Disorders	9) Plasma Cell Disorders
<ul style="list-style-type: none"> Acute Lymphoblast Leukemia (ALL) Acute Myelogenous Leukemia (AML) Acute Biphenotypic Leukemia Acute Undifferentiated Leukemia 	<p>1) Stem Cell Disorders</p> <ul style="list-style-type: none"> Aplastic Anemia (Severe) Fanconi Anemia Paroxysmal NH Congenital Cytopenia Dyskeratosis Congenita <p>2) Myeloproliferative Disorders</p> <ul style="list-style-type: none"> Acute Myelofibrosis Agnogenic Myeloid Metaplasia Polycythemia Vera Essential Thrombocythemia <p>3) Lymphoproliferative Disorders</p> <ul style="list-style-type: none"> Non-Hodgkin's Lymphoma Hodgkin's disease Polymphocytic Leukemia <p>4) Phagocyte Disorders</p> <ul style="list-style-type: none"> Chediak-Higashi Syndrome Chronic Granulomatous Disease Neutrophil Actin Deficiency Reticular Dysgenesis 	<ul style="list-style-type: none"> Mucopolysaccharidoses (MPS) Hurler's Syndrome (MPS-IH) Scheie Syndrome (MPS-IS) Hunter's Syndrome (MPS-II) Sanfilippo Syndrome (MPS-III) Morquio Syndrome (MPS-IV) Maroteaux-Lamy Syndrome (MPS-VI) Sly Syndrome, Beta-Glucuronidase Adrenoleukodystrophy Mucopolipidosis II (I-cell Disease) Krabbe Disease Gaucher's Disease Niemann-Pick Disease Wolman Disease Metachromatic Leukodystrophy <p>6) Histiocytic Disorders</p> <ul style="list-style-type: none"> Familial c Lymphohistiocytosis Histiocytosis-X Hemophagocytosis Langerhans' Cell Histiocytosis 	<ul style="list-style-type: none"> Ataxia-Telangiectasia Kostmann Syndrome Leukocyte Adhesion Deficiency DiGeorge Syndrome Bare Lymphocyte Syndrome Omenn's Syndrome Severe Combined Immunodeficiency SCID with Adenosine Deaminase Deficiency Absence of T & B Cells SCID Absence of T Cells, Normal B Cell SCID Common Variable Immunodeficiency Wiskott-Aldrich Syndrome X-Linked Lymphoproliferative Disorder <p>Other Inherited Disorders</p> <ul style="list-style-type: none"> Lesch-Nyhan Syndrome Cartilage-Hair Hypoplasia Glanzmann Thrombasthenia Osteopetrosis Adrenoleukodystrophy Ceroid Lipofuscinosis Congenital Erythropoietic Porphyria Sandhoff Disease 	<ul style="list-style-type: none"> Multiple Myeloma Plasma Cell Leukemia Waldenstrom's Macroglobulinemia Amyloidosis <p>Abnormalities</p> <p>1) Inherited Platelet Abnormalities</p> <ul style="list-style-type: none"> Congenital Thrombocytopenia <p>2) Inherited Erythrocyte Abnormalities</p> <ul style="list-style-type: none"> Beta Thalassemia Major Sickle Cell Disease Blackfan-Diamond Anemia Pure Red Cell Aplasia <p>Other Malignancies</p> <ul style="list-style-type: none"> Ewing Sarcoma Neuroblastoma Renal Cell Carcinoma Retinoblastoma Brain tumor Ovarian Cancer Small Cell Lung Cancer Testicular Cancer
<p>2) Chronic Leukemia</p> <ul style="list-style-type: none"> Chronic Myelogenous Leukemia (CML) Chronic Lymphocytic Leukemia (CLL) Juvenile Chronic Myelogenous Leukemia (JCML) Juvenile Myelomonocytic Leukemia (JMML) <p>Syndromes</p> <ul style="list-style-type: none"> Myelodysplastic Syndromes Amyloidosis Chronic Myelomonocytic Leukemia (CMML) Refractory Anemia (RA) Refractory Anemia with Excess Blasts (RAEB) Refractory Anemia with Excess Blasts in Transformation (RAEB-T) Refractory Anemia with Ringed Sideroblasts (RARS) 				

Gelecek Kök Hücre ile gelecek....



İnsan embriyonik kök hücresi (hESC) tedavisi olmayan birçok hastalıkta ümit olmaya devam ediyor..... Spinal kord yaralanmaları, ALS, Alzheimer's, Parkinson's, vs.

Doku tamiri ve replasman



Felçler



Kalp Krizi



Eklem hast



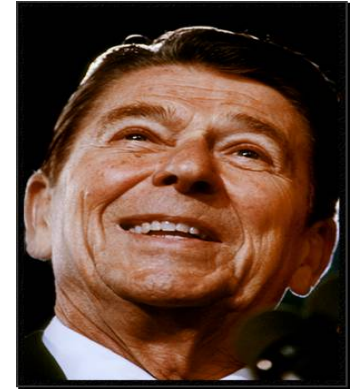
Diyabet



Burger

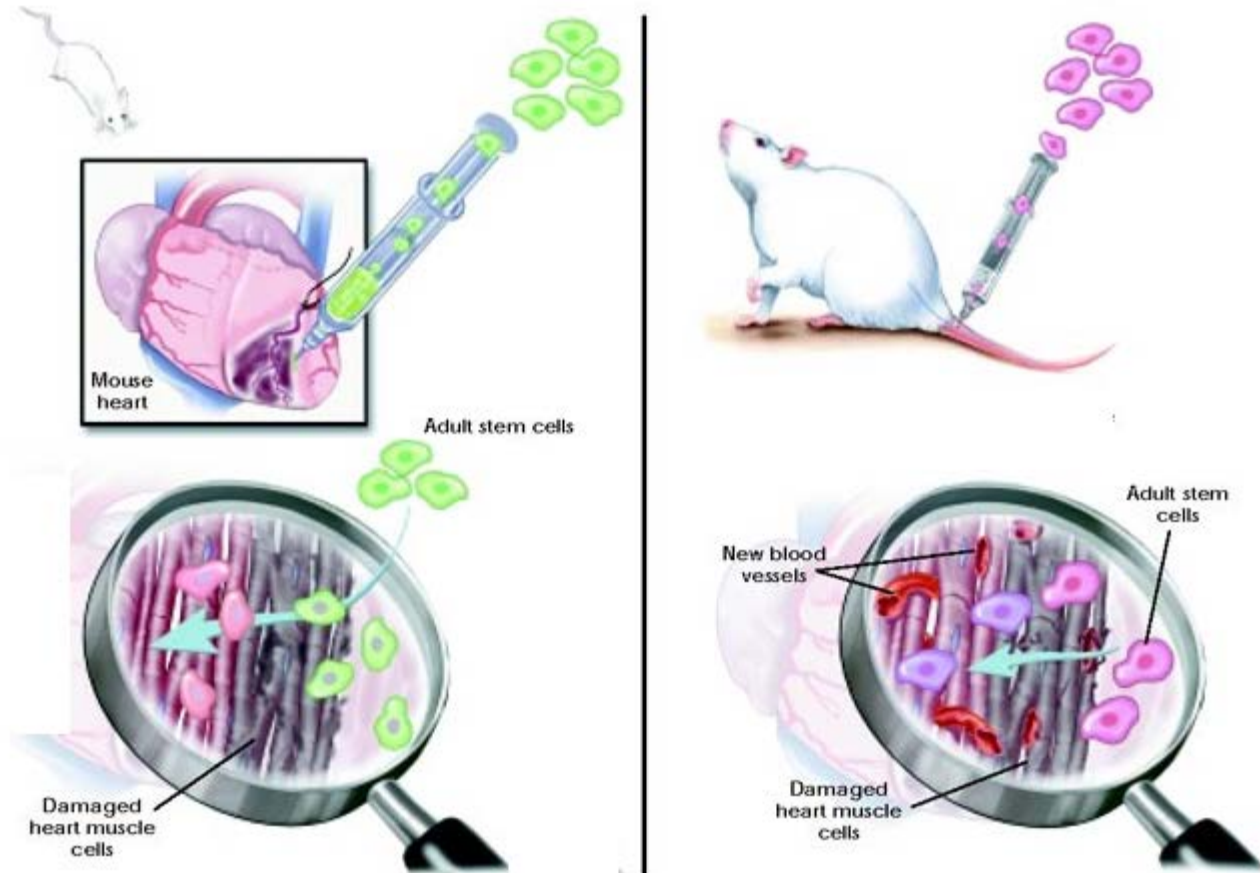


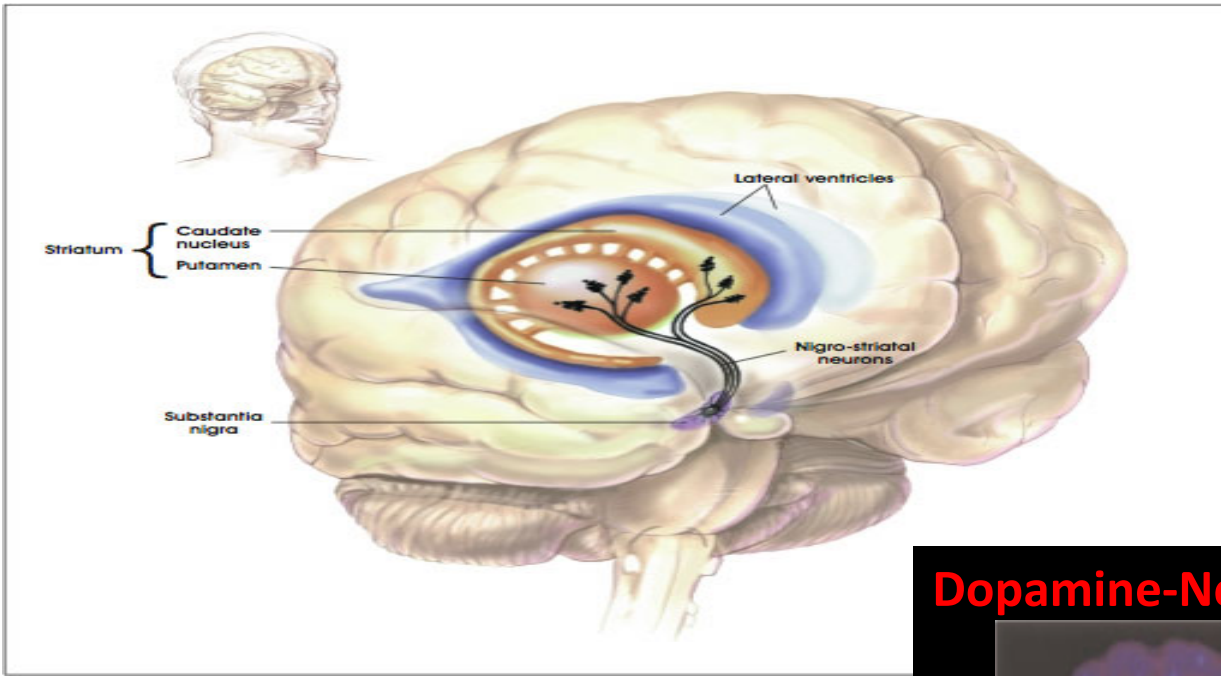
Parkinson



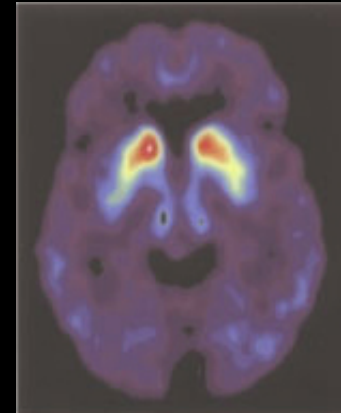
Alzheimer

Kök Hücreyi nasıl uygulayalım...???

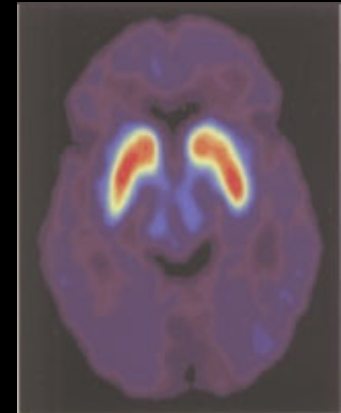




Dopamine-Neuron Transplantation



Before Surgery



After Surgery

Beyin Onarımı

Spinal Kord Yaralanmalarında Kök Hücre Tedavileri

Hayvan modeli çalışmalarından sonra Klinik çalışmalar başlatılmıştır.

Başlama

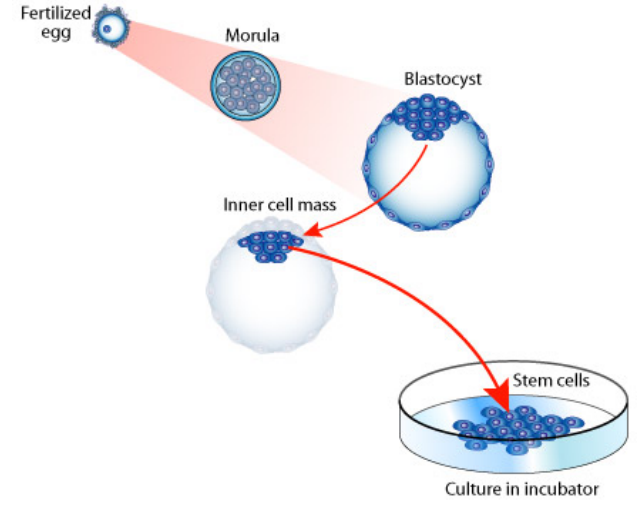
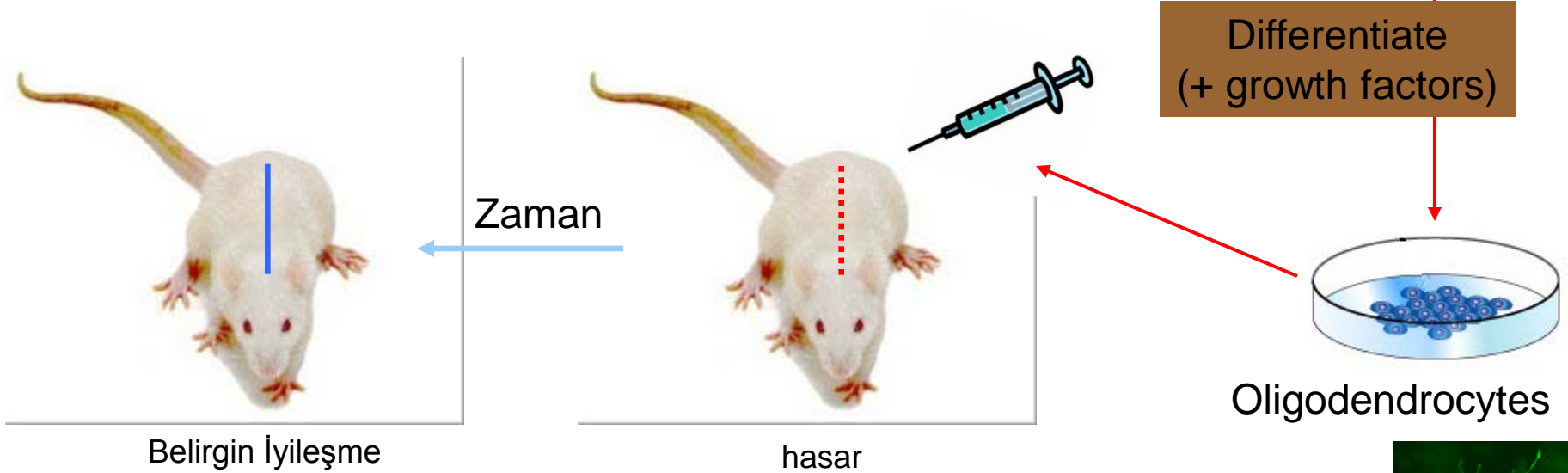
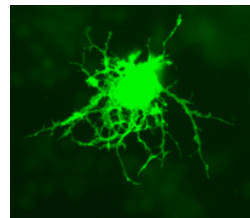


Illustration by [Cell Imaging Core](#) of the Center for Reproductive Sciences.



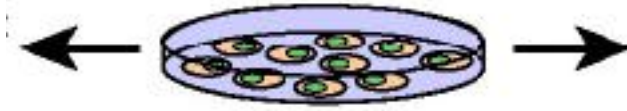
*Tedavi beklentisi kronik paralizi vakalarında daha düşük..





Kök Hücre Tedavilerini Geleceği

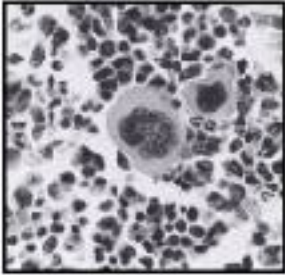
İlaç gelişimi
ve toksisite
çalışmaları



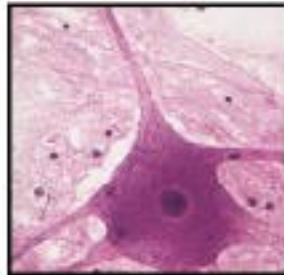
Kök Hücre
Kültürleri

Deneysel
Araştırma ve
Denemeleri
(örn.gen kontrol)
Çalışmaları

Hücre-doku tedavileri



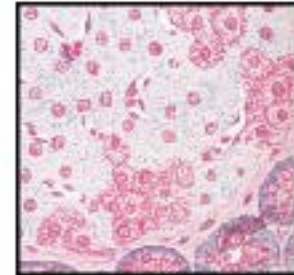
Kemik İliği



Sinir Sistemi



Kalp Kası



Pankreas

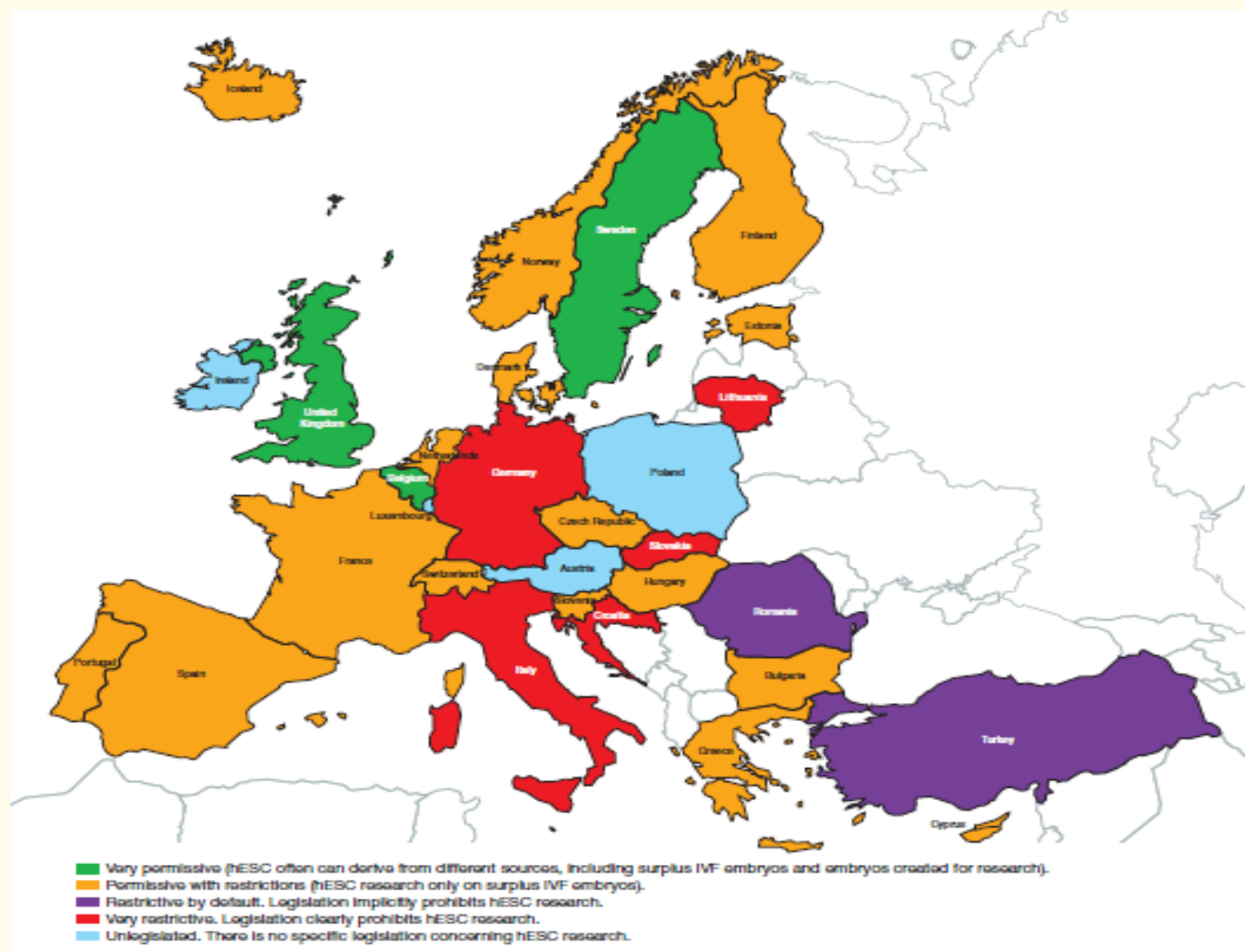


Figure 1. National positions on human embryonic stem cell research policy and regulatory framework in Europe.

Hematopoetik Kök Hücre nakli

Avrupa KIT aktivitesi 2010

HSCT - rates in Europe 2010

Total transplants (all)

per 10 million

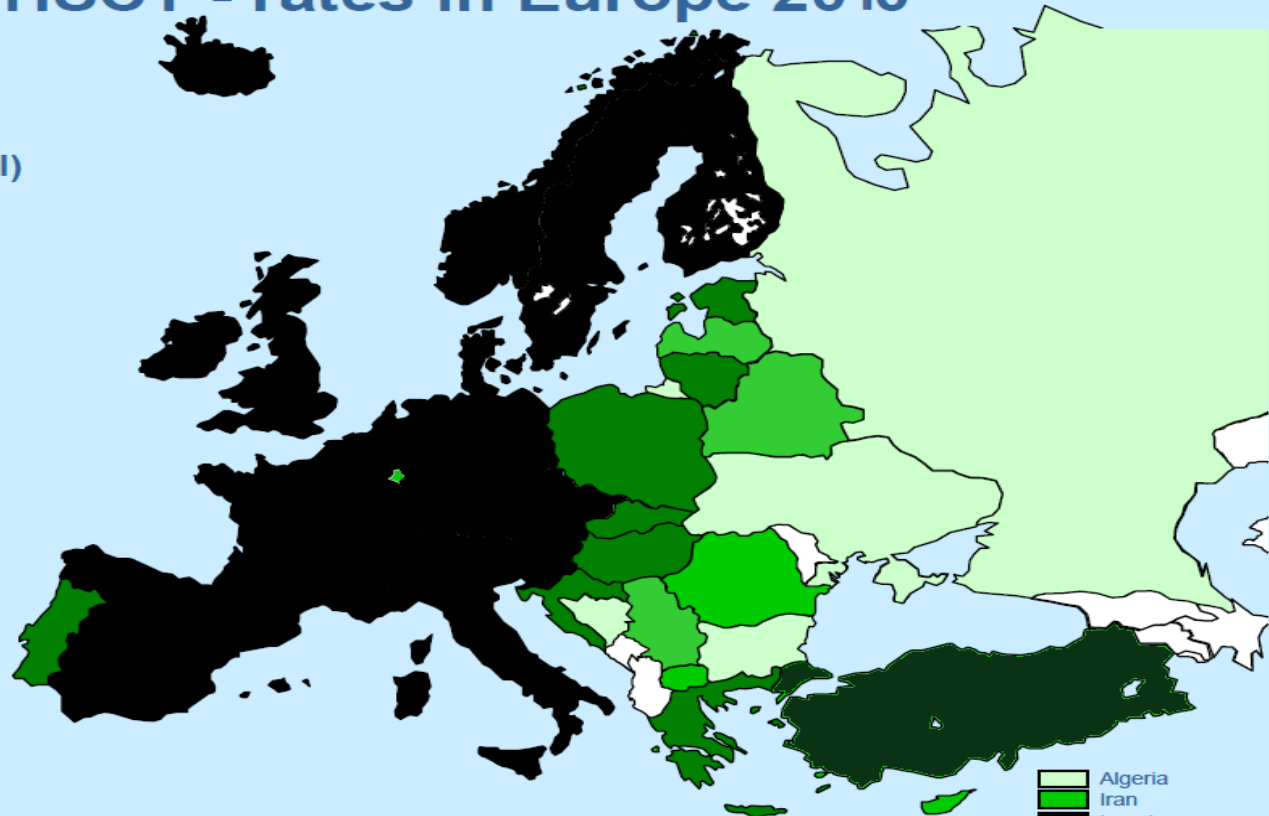
0 or no report

1 - 50

51 - 200

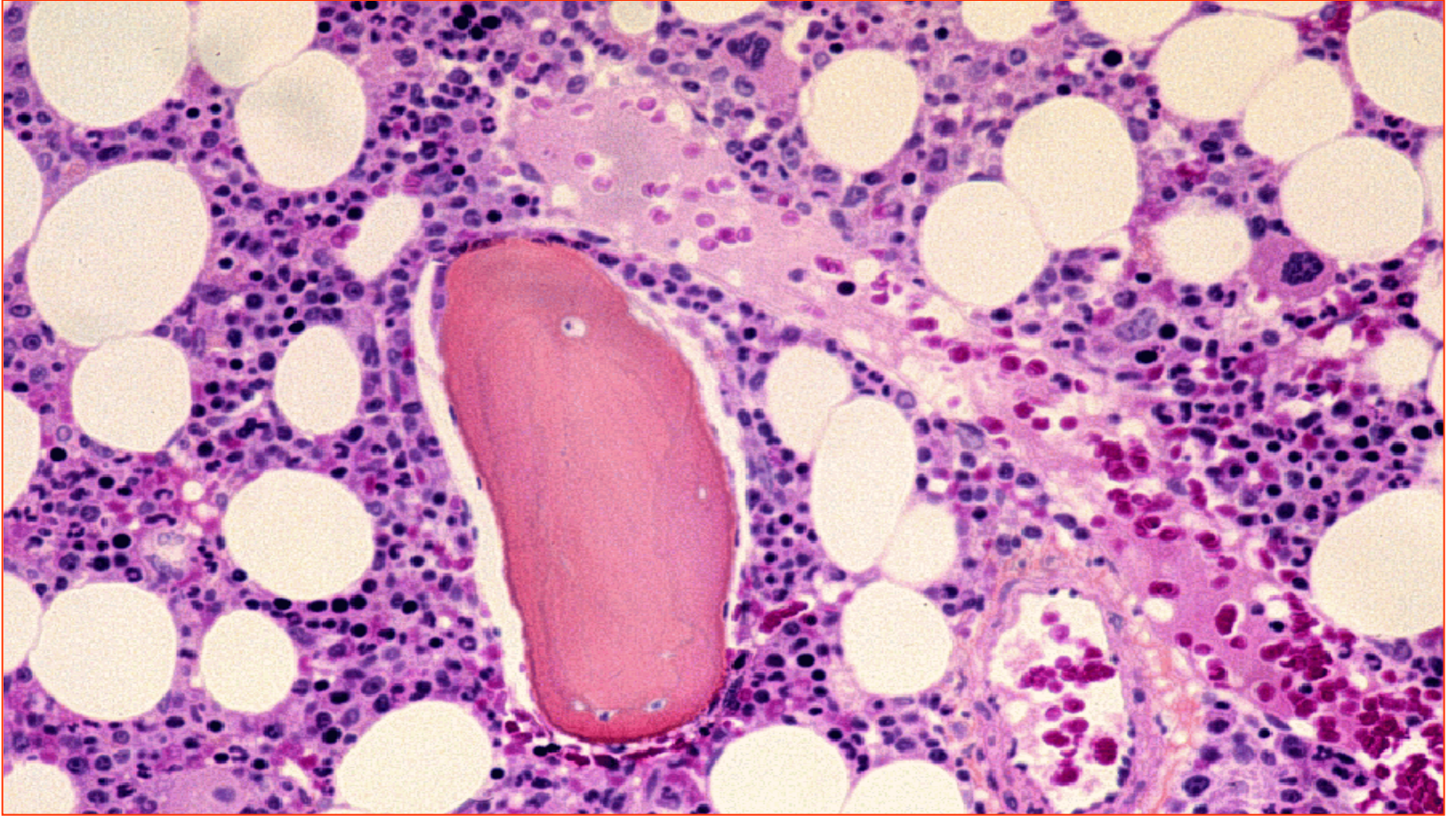
201 - 400

> 400

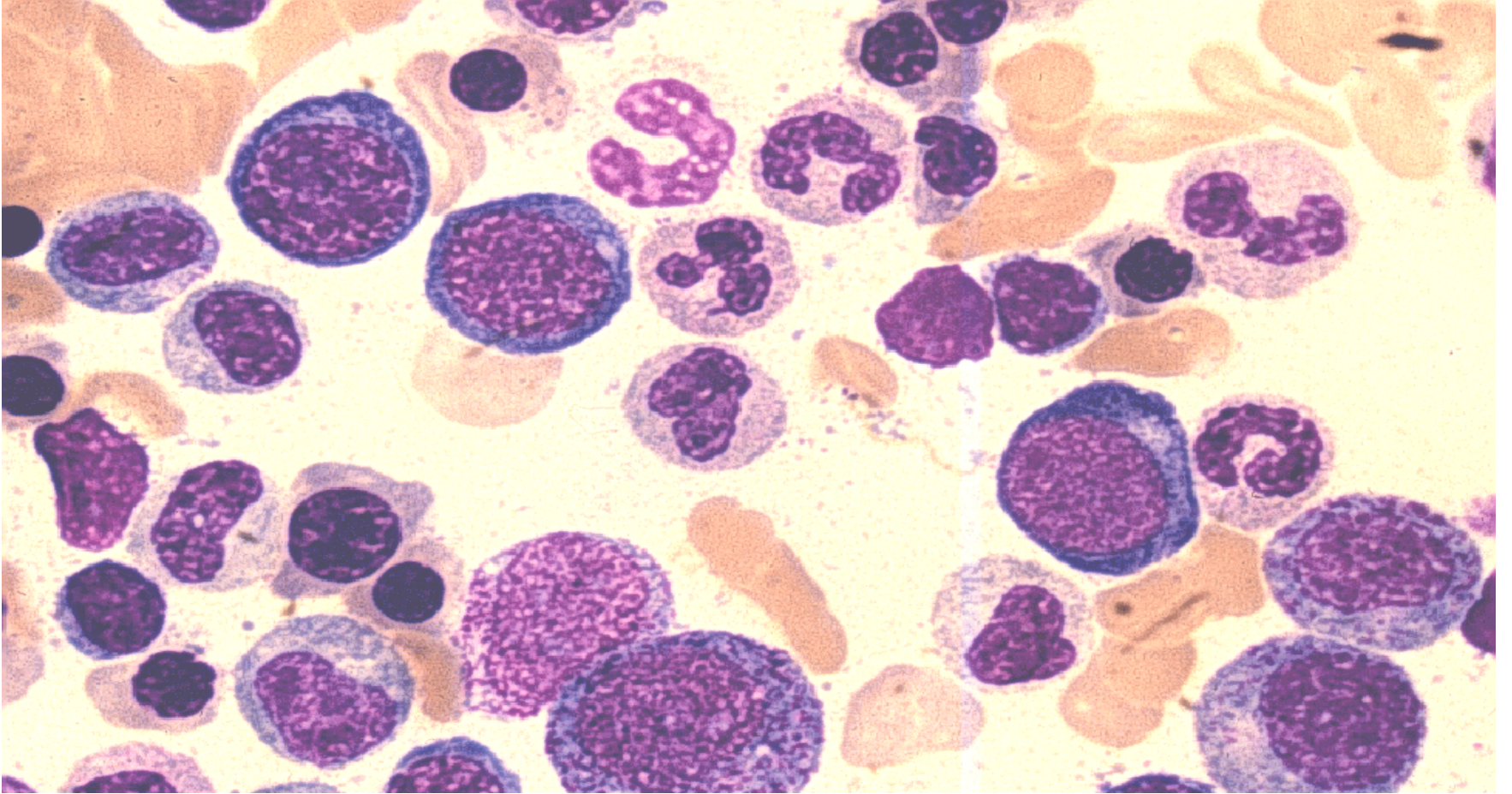


- Algeria
- Iran
- Israel
- Lebanon
- Saudi Arabia
- South Africa
- Tunisia
- Jordan

Kemik İliđi: Fonksiyon

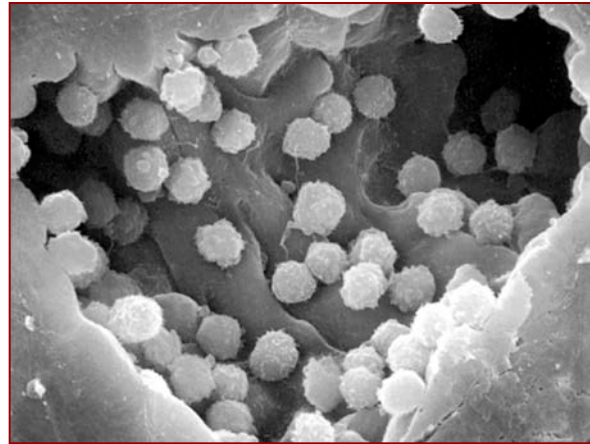
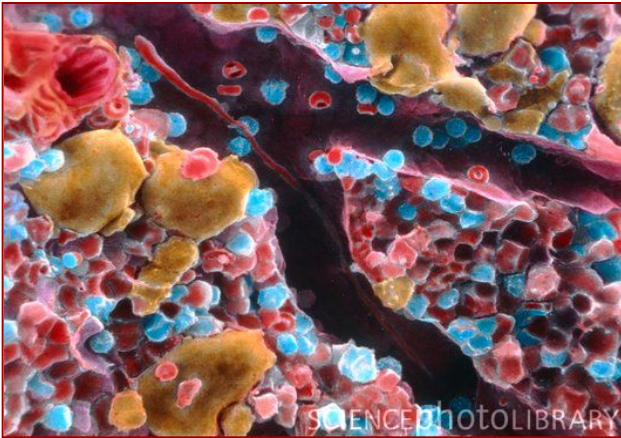


Kemik İliđi: Fonksiyon



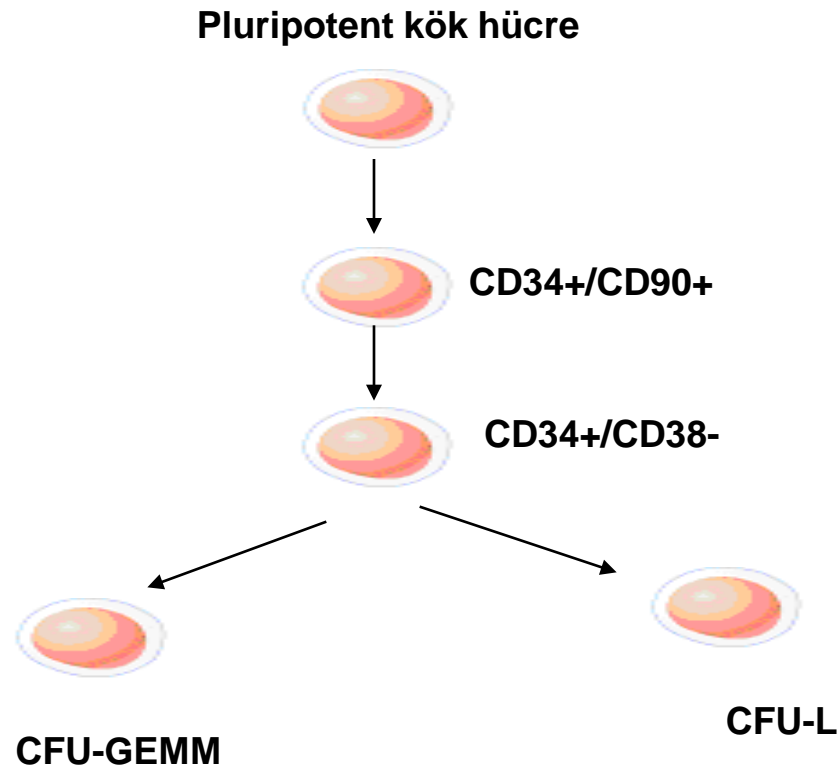
Kemik İliđi: Fonksiyon

- Kan hücrelerinin üretimi,
 - 175 milyar kırmızı küre/gün
 - 70 milyar beyaz küre/gün (neutrophils, eosinophils, basophils)
 - 175 milyar kırmızı küre/gün
 - Üretim kapasitesini ihtiyaç halinde 10 katı artırabilir...

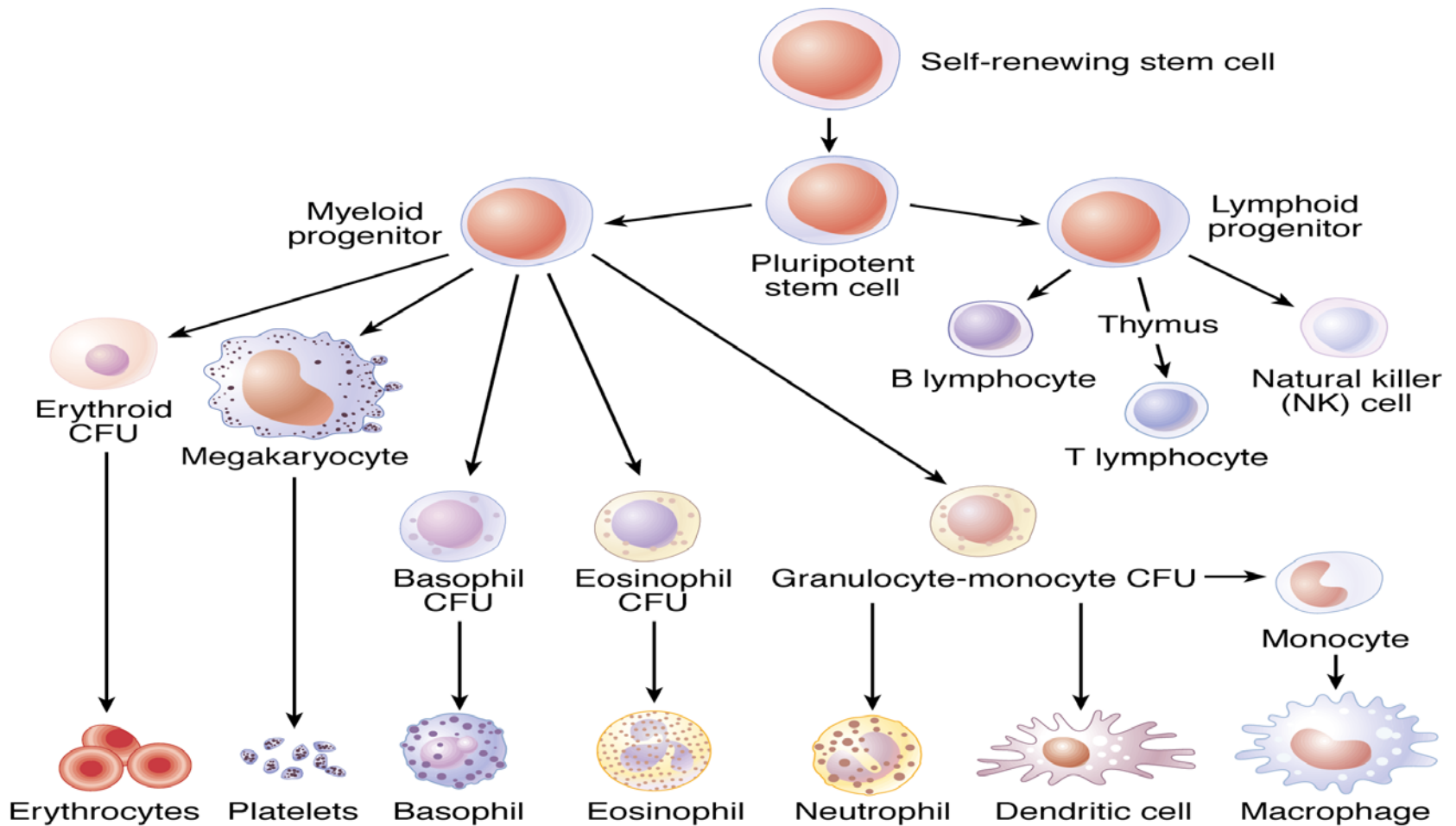


kemik iliđinde
hücrelerin %1- 0.1'i
Kök hücre ve
öncülleridir.

Erken Hematopoetik kök hücre modelleme

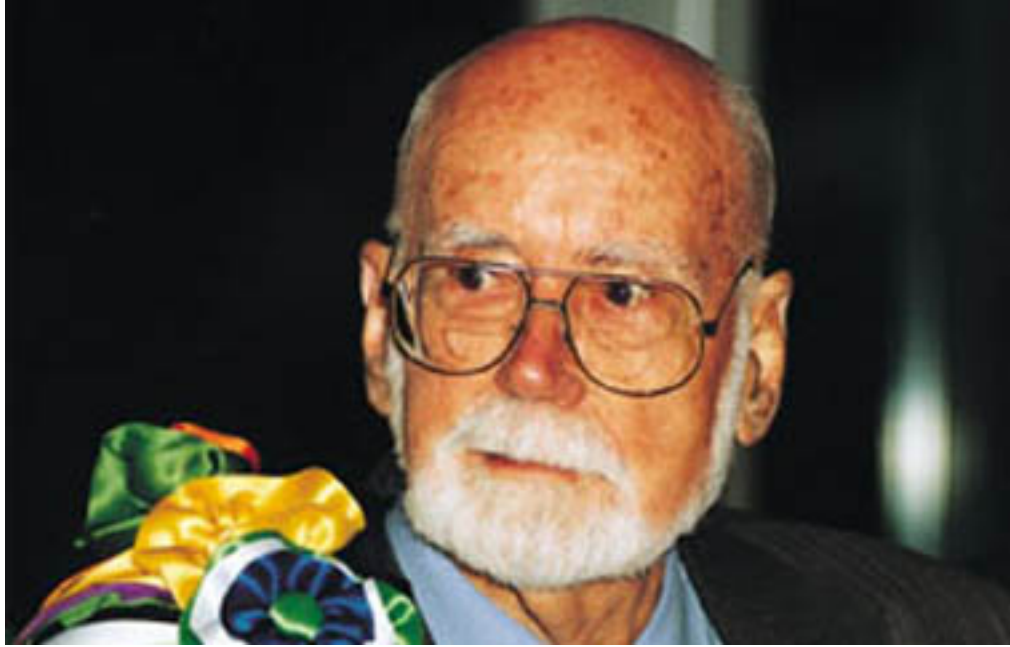


Hematopoez



The Nobel Prize, 1990

E. Donnall Thomas



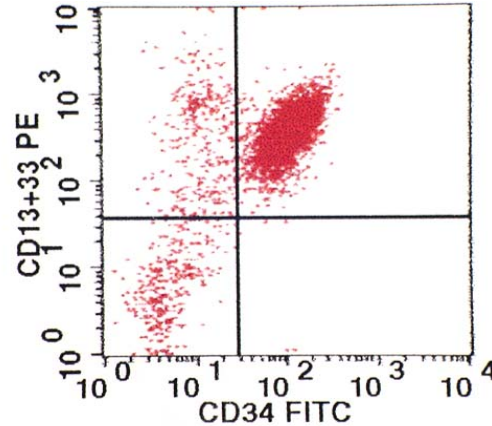
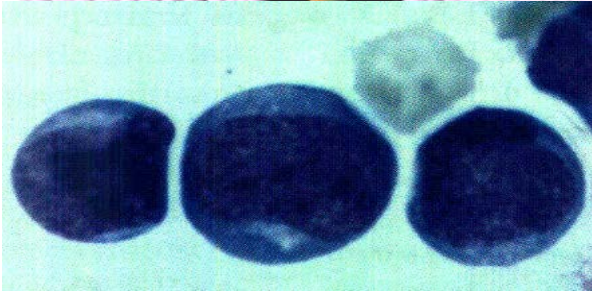
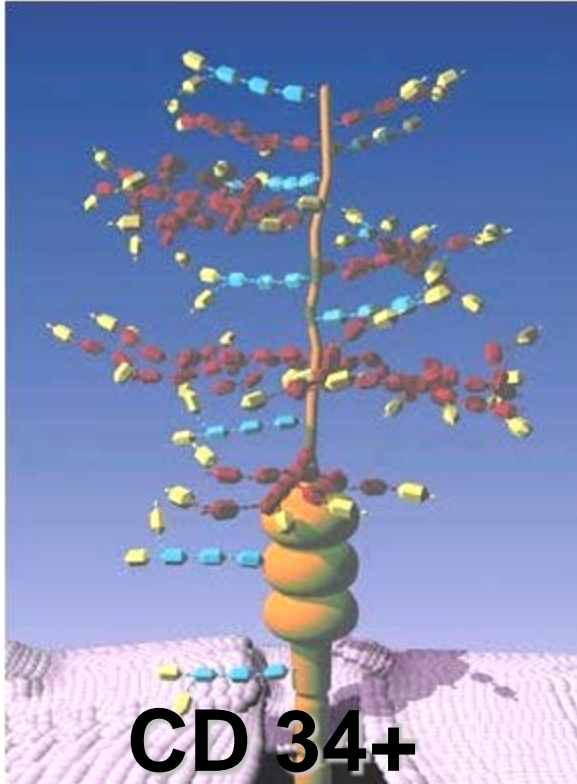
Akut lösemide ilk başarılı kök hücre nakli

Thomas ED, Lochte HL, Lu WC, Ferrebee JW. Intravenous infusion of bone marrow in patients receiving radiation and chemotherapy. N. Engl. J. Med. 1957; 257: 491.

HKH'nin kimlik numarası : CD 34

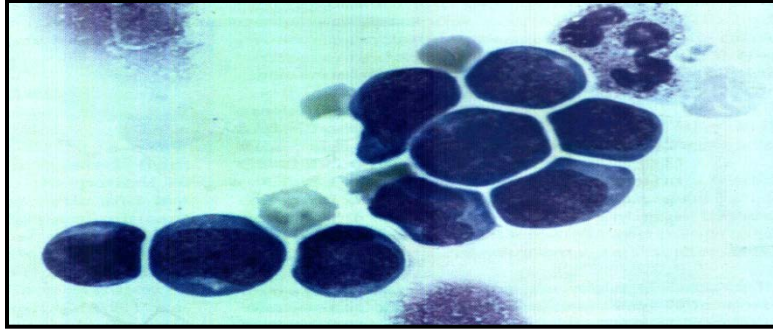
•**CD43:** 105-120 kDa ağırlığında membran glikoprotein

- Erken hemapoetik kök hücre işaretleyicisi
- CD34: Periferik MNH'lerin % 0.1
Kemik iliği MNH'lerinin % 1-4



Hematopoetik kk hcre toplama

CD34+ hcrelere nasıl ulařırız..



- Kemik ilięinden toplama
- evre kanına hareketlendirilen hcrelerin toplanması

Kemik İliğinden toplama

- Genel anestazi
- İlik pelvik kemiklerden alınır
- Artıklar filtre edilir
- Donmuş veya taze ürün olarak hastaya uygulanır.

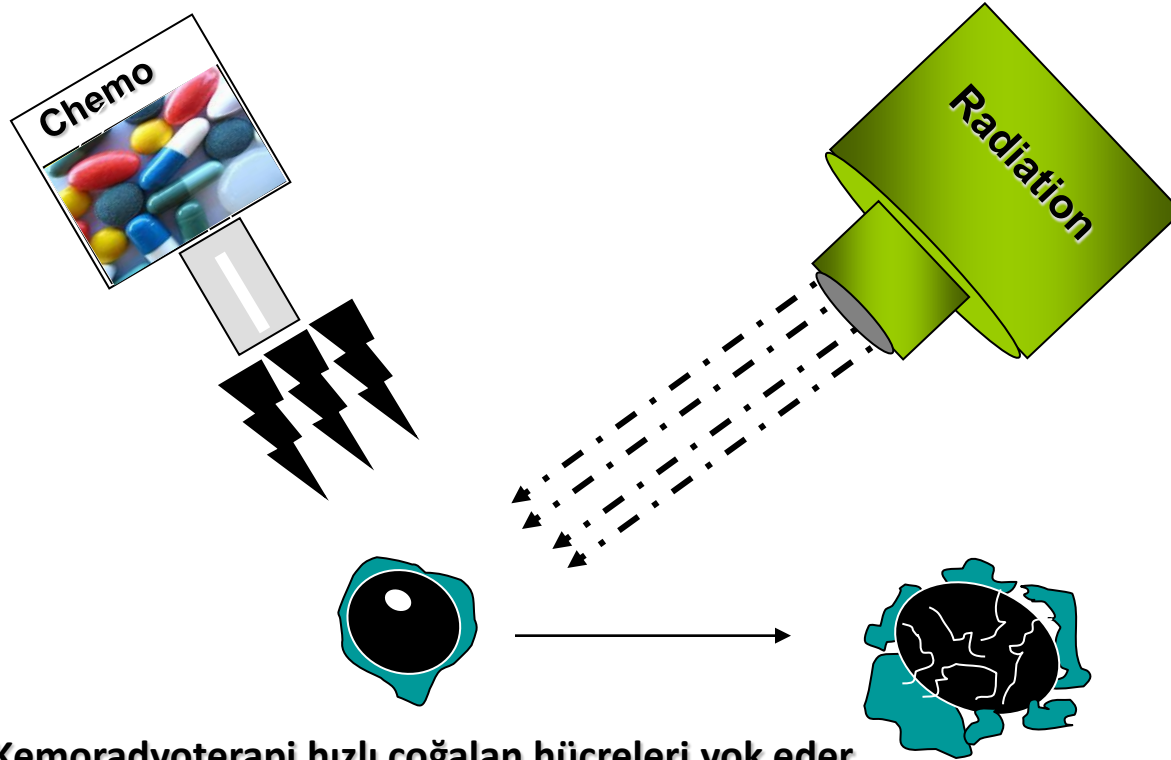


Çevre kanı kök hücresi toplama

- **Kök hücre ilikten çevreye gönderilir**
 - G-CSF
(sağlıklı verici)
 - Cyclophosphamide + G-CSF in
(hasta)
- **5.gün (sağlıklı verici)den, yaklaşık 10-132 günde hastadan toplanır**
 - İşlem 2- 3 saat kadar sürer
- **Taze ürün veya dondurulmuş olarak kullanılır...**



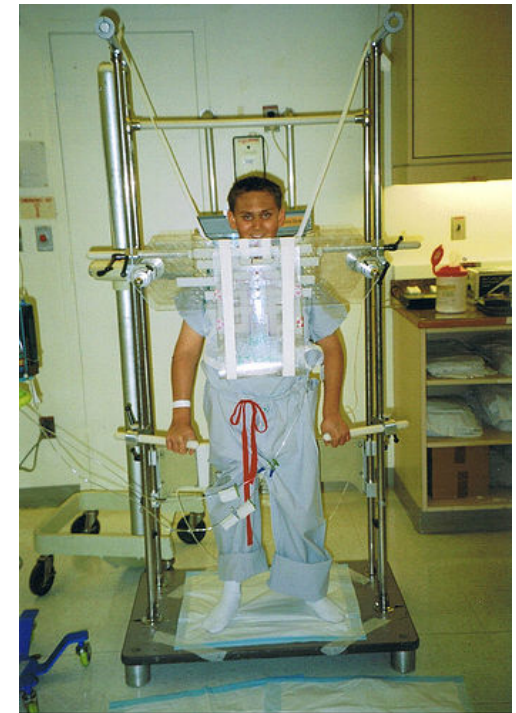
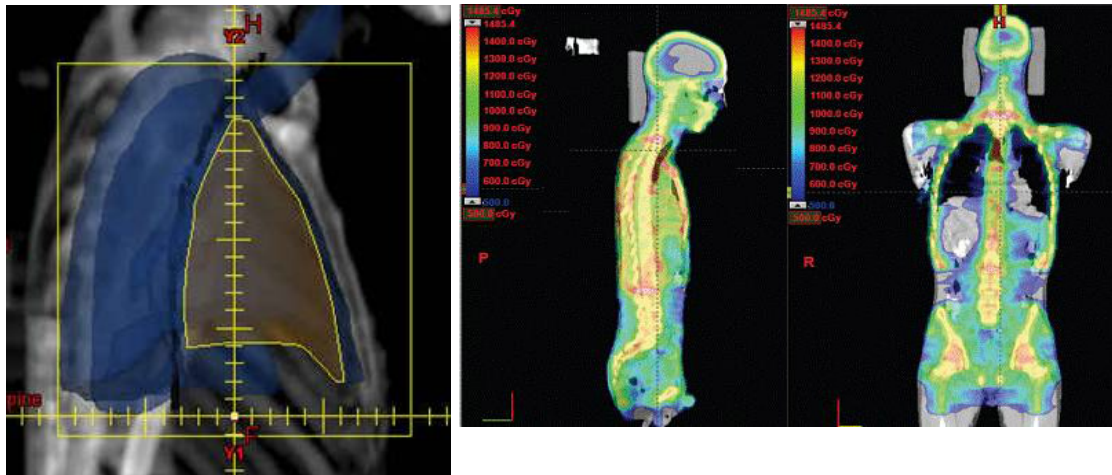
Kök Hücre nakline hazırlık tedavisi ile bir taraftan ilik mesafesi boşaltılarak yuvalanmaya hazır hale getirilirken; bu uygulama myeablatif dozda kemoradyoterapi imkanı sağlar...



Kemoradyoterapi hızlı çoğalan hücreleri yok eder

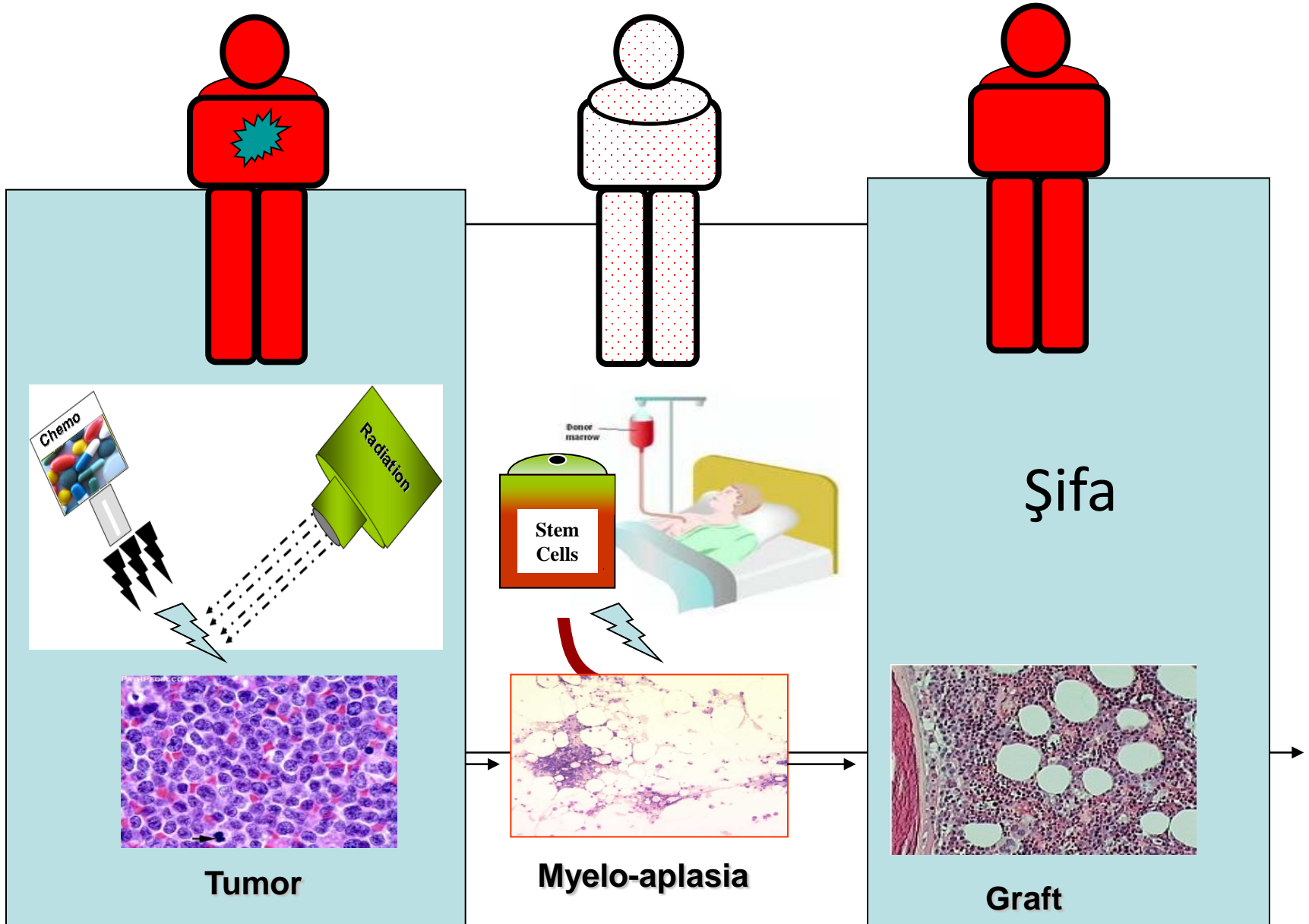
Myelo-ablation

- Total body irradiation 10-12 Gy (fractionated) + cyclophosphamide
- Cyclophosphamide + busulfan

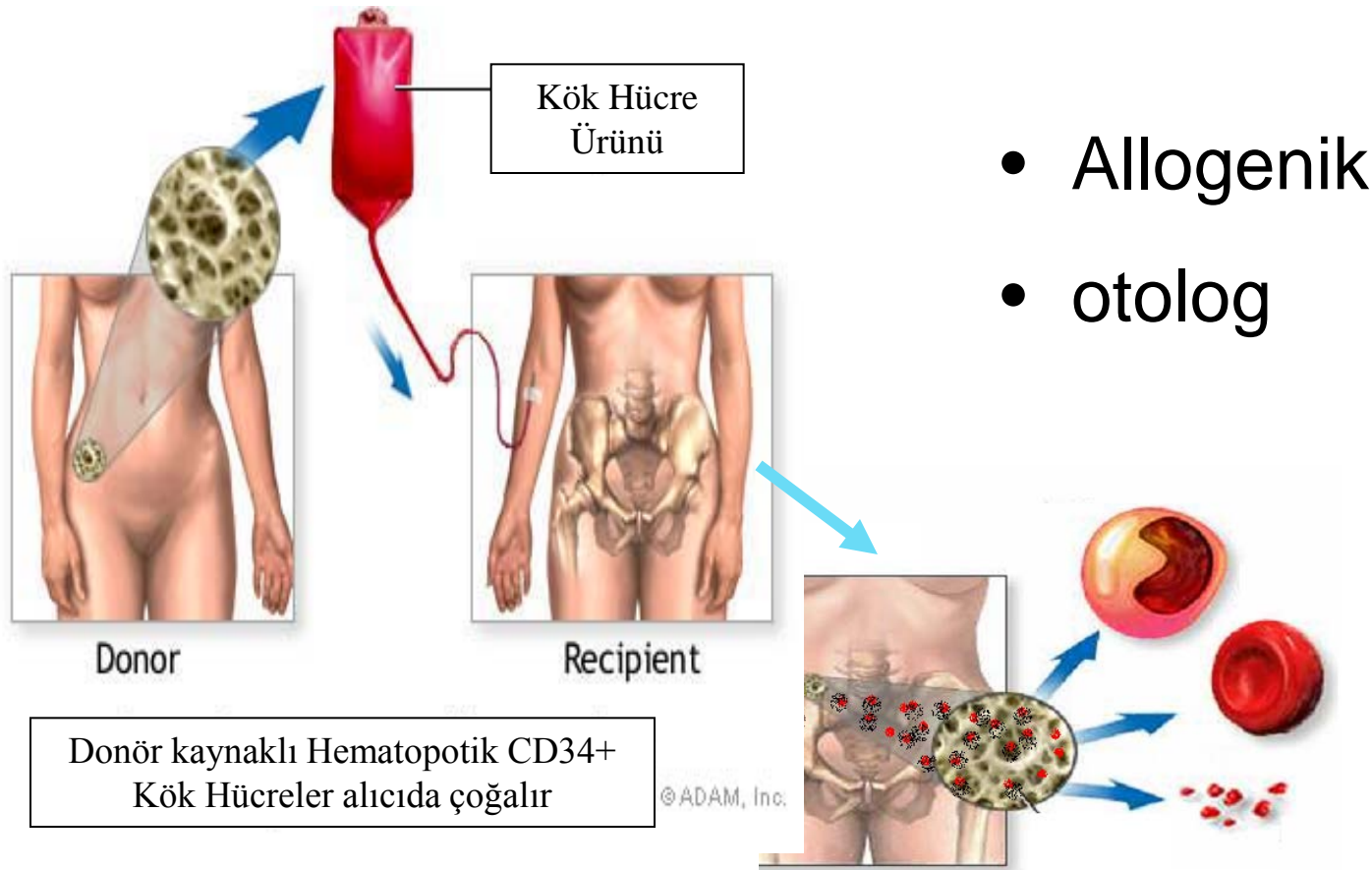


Nb 4.5 Gy fatal in 50% exposed individuals

İlik naklinin mantığı



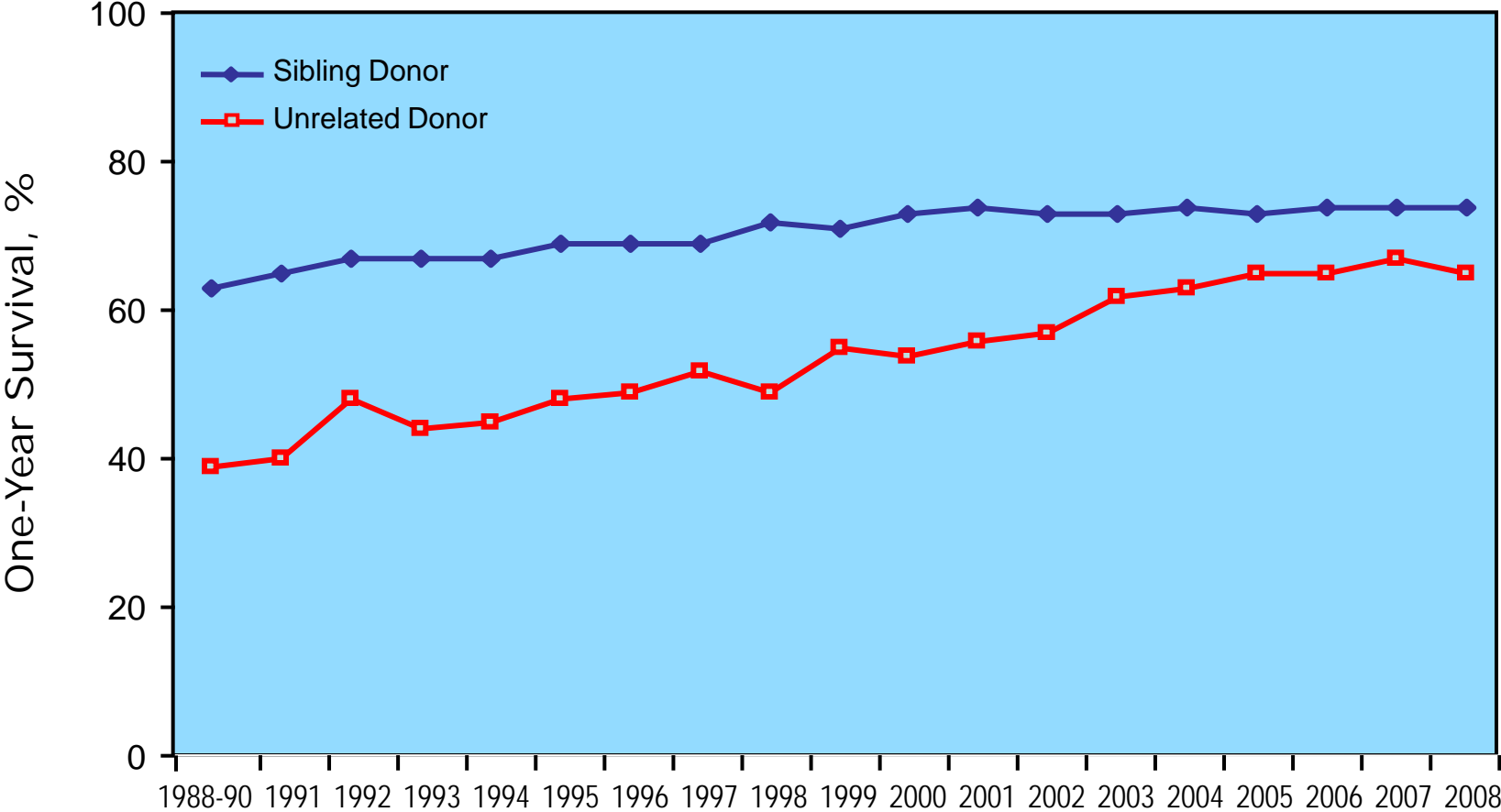
Kök hücre (ilik) naklinin tipleri....



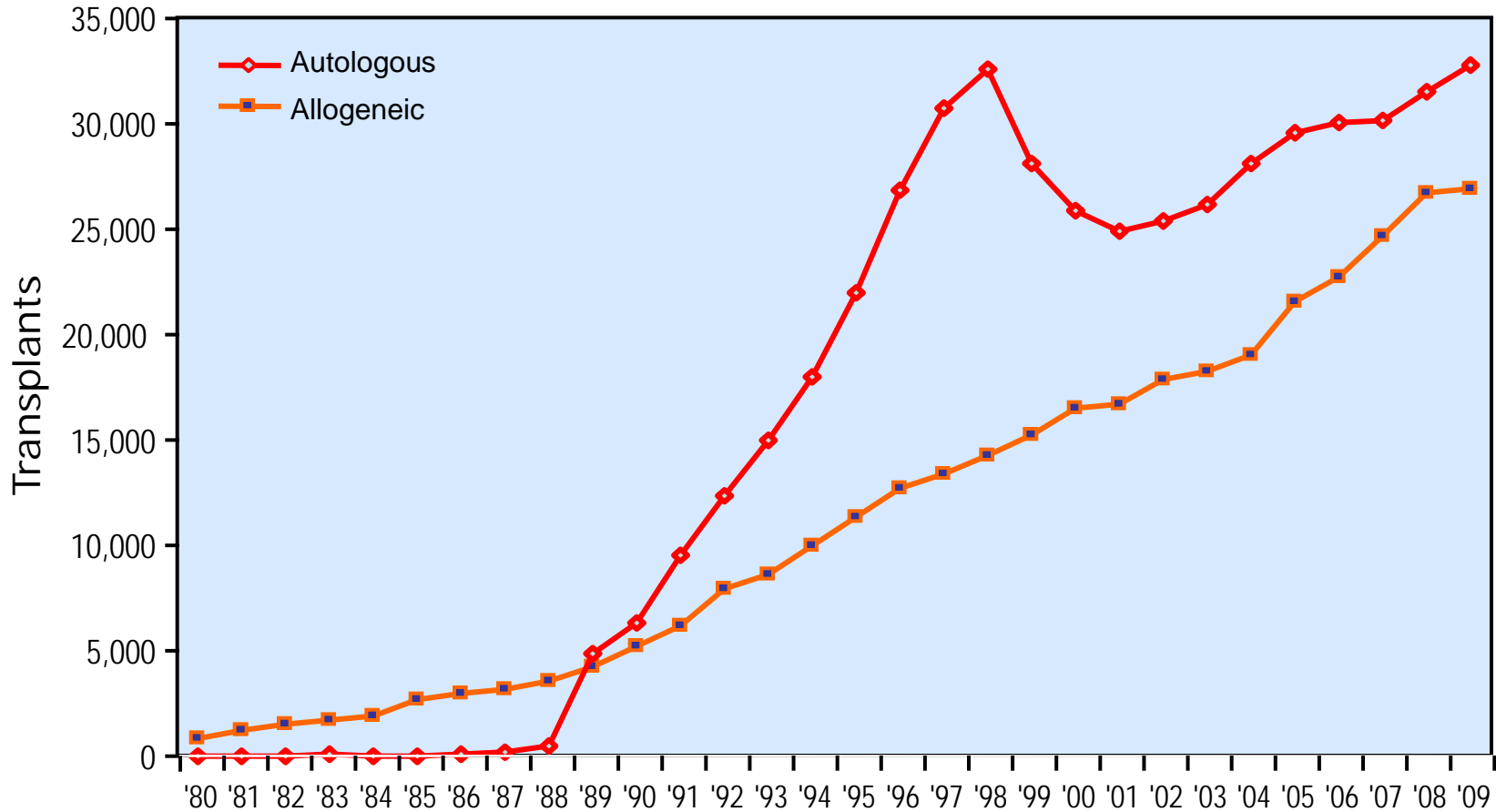
HKH tedavi endikasyonları

- Leukemias (acute and chronic)
- Lymphomas (Hodgkin's and non-Hodgkin's)
- Multiple myeloma
- Myelodysplastic and myeloproliferative disease
 - (myelofibrosis, polycythemia vera, essential thrombocytosis)
- Aplastic anemia
- Metastatic breast cancer *
- Some metabolic diseases
- childhood cancers (neuroblastoma, sarcomas, high grade gliomas, Wilm's tumor)
- Congenital immunodeficiencies (CGD, SCID, Wiskott-Aldrich)
- Rheumatologic/autoimmune diseases (RA, jRA, Lupus, AIHA)
- Hemoglobinopathies
- Metabolic diseases (osteopetrosis, Hurler's, adrenaleukodystrophy)

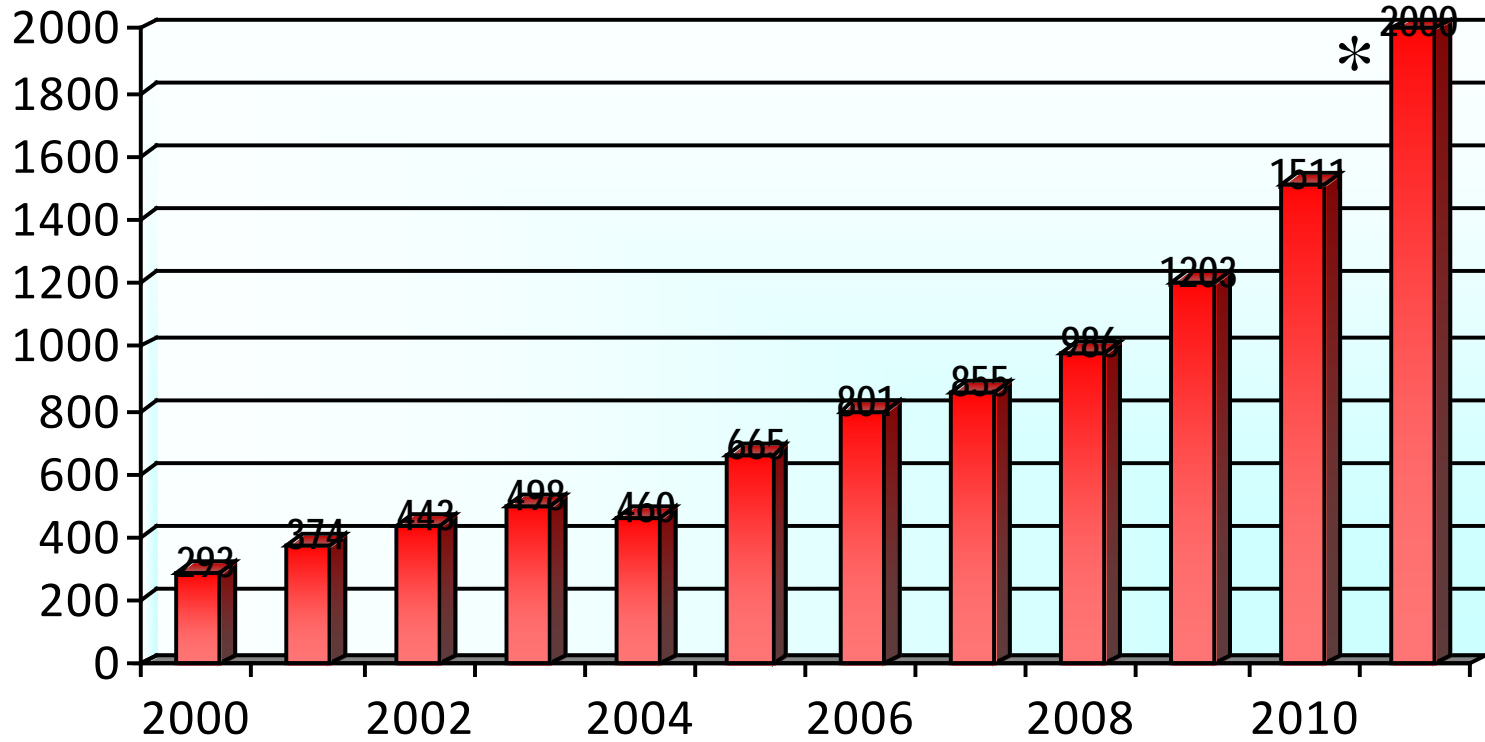
Trends of transplant survival RATE & succes , age <50 years, by year of transplant and graft source, 1988-2008



Transplant Activity Worldwide 1980-2009



Türk merkezlerin 2012 aktiviteleri : Kök hücre nakli sayısı

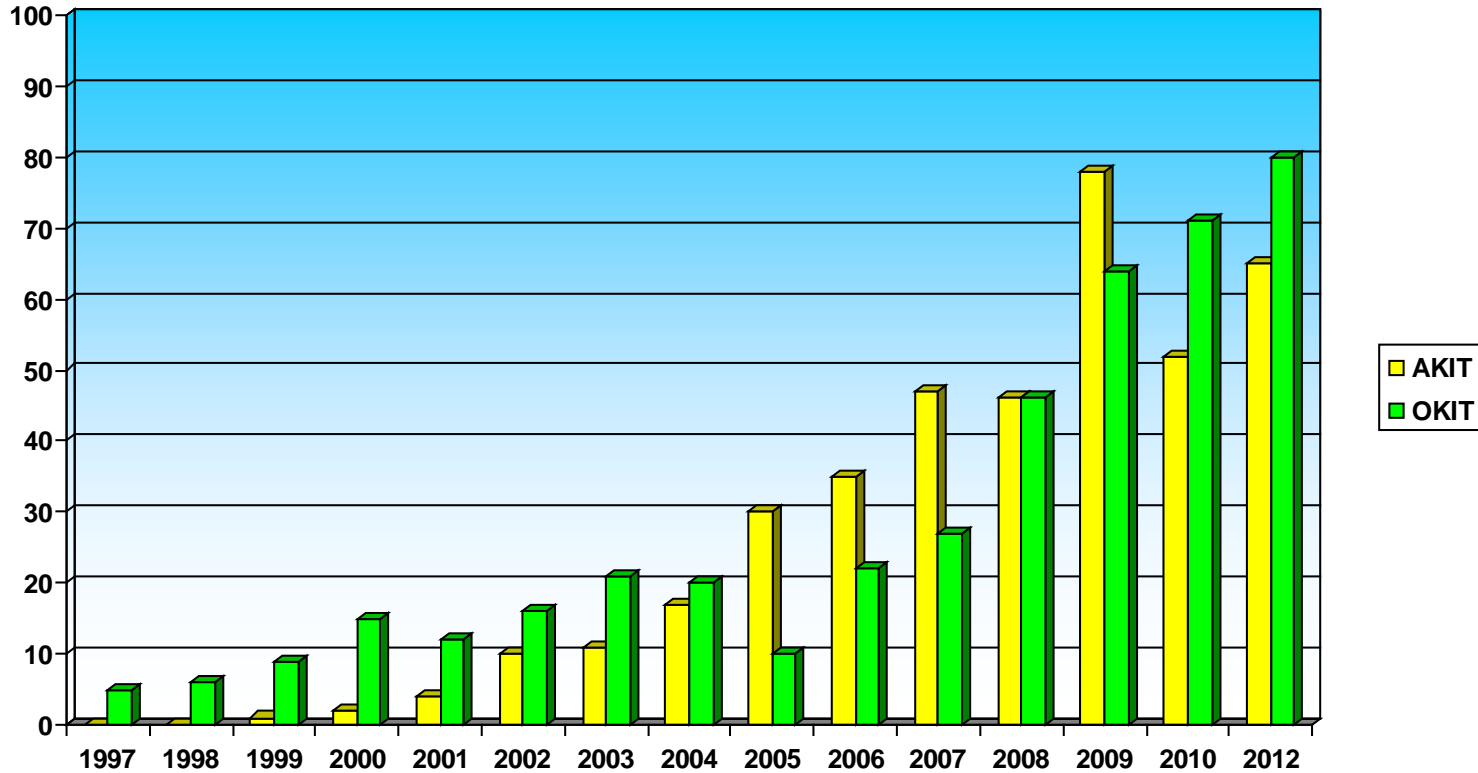




Erciyes University

Cappodocia Transplant Center (EBMT: cic 623 & CIBMTR cic: 783)

Hematopoietic Stem Cell Transplantation Activity Survey



Erciyes University

Cappadoccia Transplant Center (EBMT: cic 623 & CIBMTR cic: 783)

Hematopoetic Stem cell Transplatation Activity Survey



Yaşama
Dair Herşey...



GEN KÖK

Genom ve Kök Hücre Merkezi
Genome and Stem Cell Center





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Hmş. Gülbahar CİLAVDAROĞLU

