ANKARA ÜNİVERSİTESİ
BİYOTEKNOLOJİ
ENSTİTÜSÜ

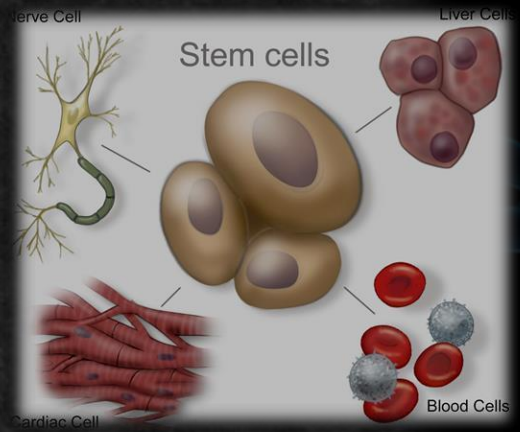
ANKARA ÜNİVERSİTESİ 1946

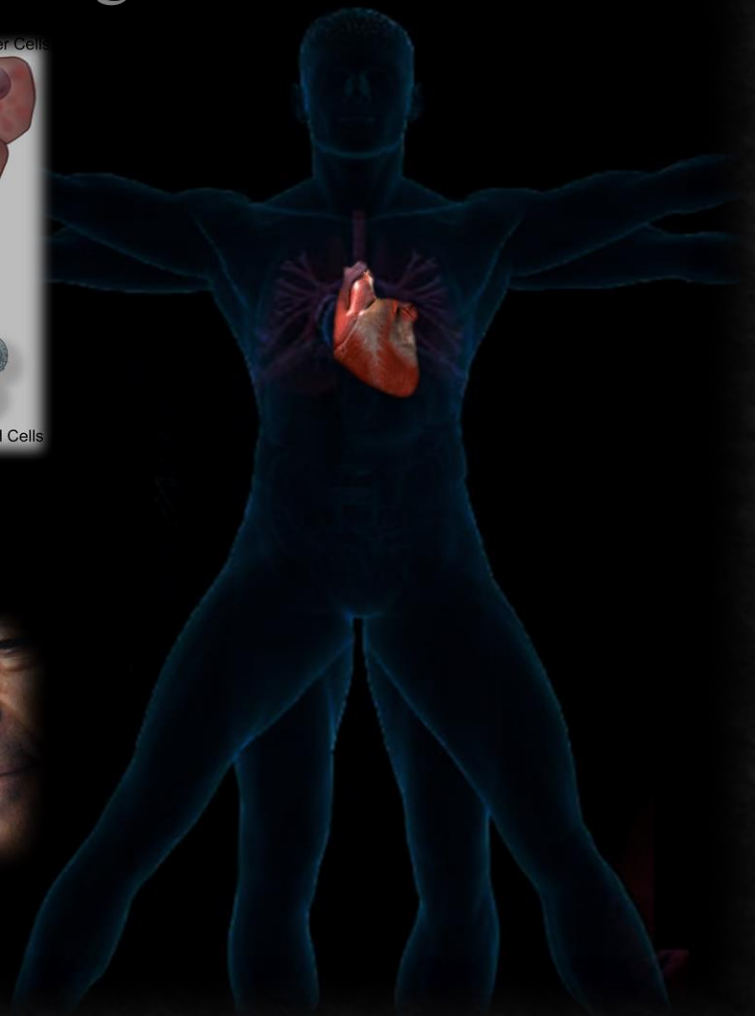
ANKARA UNİVERSİTY
BİOTECHNOLOGY INSTİTUTE

Regenerative Medicine

Onarımsal Tıp

(Rejeneratif Tıp)





STEP 1: Establishment of Cell Culture

Isolation of source cells → Culturing of cells

STEP 2: Generation of iPSC

Yamanaka's Cocktail (Oct4, Sox2, Klf4 and c-Myc)

Source Cells

Feeder cells

iPSC

Methods for Delivery of Transcription Factors

Integrating Viral Vector Systems

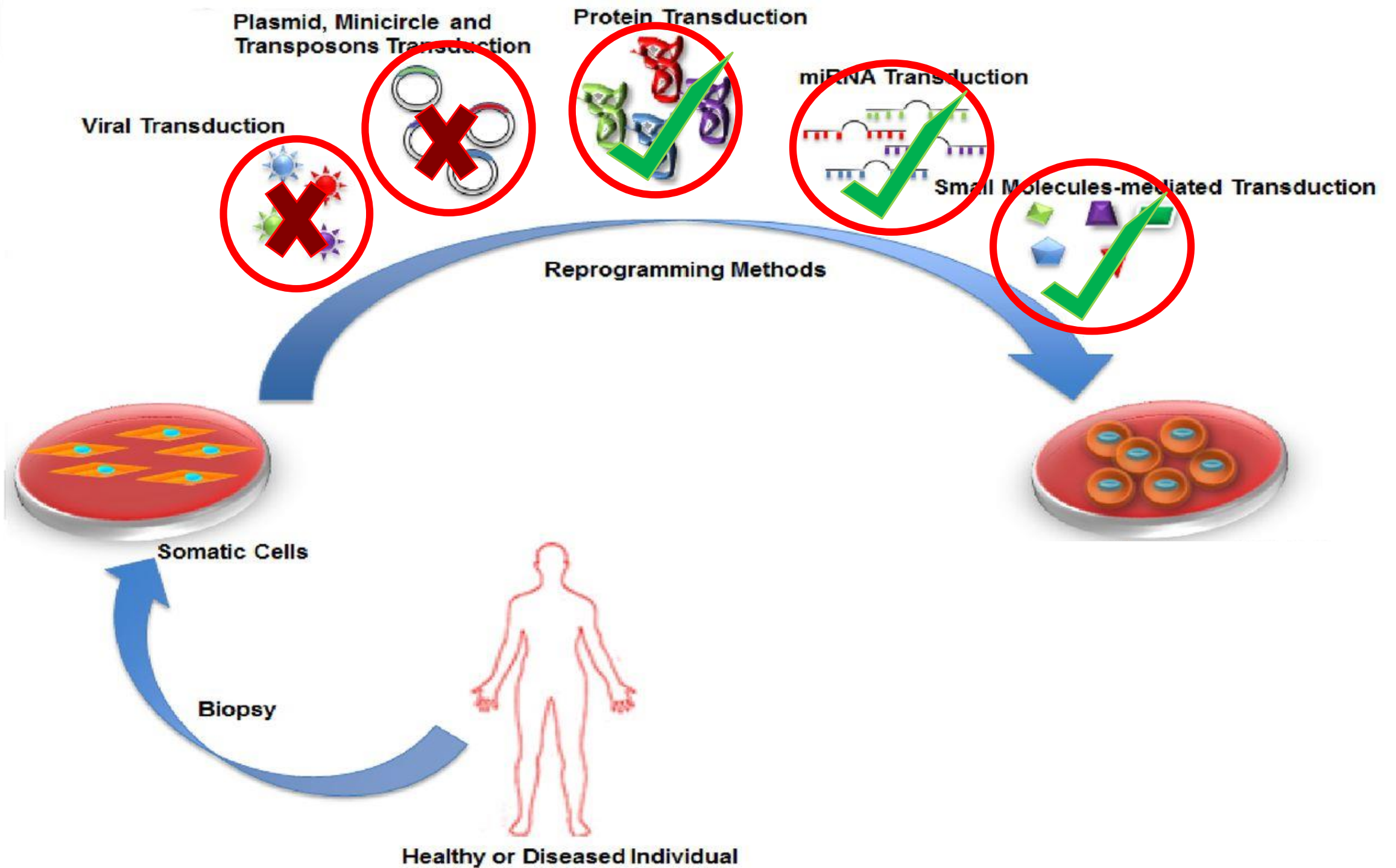
- Retroviral
- Lentiviral
- Inducible Lentiviral

Integration Free Systems

- Viral Vectors
- Plasmid DNA
- Recombinant Proteins
- Synthetic mRNA

STEP 3: Characterization and Expansion of iPSC

Characterization and expansion of iPSCs formed →


Plasmid, Minicircle and
Transposons Transduction
Protein Transduction
Viral Transduction
miRNA Transduction
Small Molecules-mediated Transduction
Reprogramming Methods
Somatic Cells
Biopsy
Healthy or Diseased Individual

DNA kullanılmayan metotlar (DNA- free methods)

- Yamanaka faktörlerinin proteinlerini kullanmak
- Yamanaka faktörlerinin mRNA‘larını kullanmak
- Direkt yeniden programlama

Klinikte kullanılabilir uPK hücre elde etme yöntemleri

iPS hücelerinin dezavantajlarının azaltılması ….

1) kullanılan transkripsiyon faktörlerini en aza düşürmek;

Örneğin: c-Myc ……..onkogen

2) uPK hücrelerinin üretiminde güvenilebilir yöntemler veya entegre olmayan yöntemlerin kullanılması (integration free iPS);

	Advantages	Disadvantages
Forced expression of genes via retrovirus	Well-characterized method, long history of use, arguably a simple approach and low cost, relatively high reprogramming rates of 0.01–0.02%	Integration into the genome may generate immunogenic cells, virus will only enter cells in mitosis, use of oncogenes such as c-Myc
Small molecules	Low cost of compounds, increases the efficiency of reprogramming	Only recent reports of full reprogramming achievable with small molecules alone: further characterization of lines generated needed
Synthetic miRNA	No integration within the genome	Very low reprogramming efficiency, miRNA degrades rapidly, modification of miRNA complicated, and time-consuming
Forced expression of genes via Sendai virus	No integration into the genome, higher efficiency of reprogramming than using retrovirus, diluted out of culture upon passage rapidly, high reprogramming rate of 0.1%	Difficult to work with, therefore most commonly used as pre-packaged "kits," which are expensive compared to other viral methods of reprogramming
Episomal plasmid vector system	No genomic footprint	Very low efficiency of reprogramming (0.0002%), loss of episomal plasmid
Stimulus-triggered acquisition of pluripotency (STAP)	No nuclear transfer or introduction of transcription factors	Limited capacity for self-renewal when compared to ES cells. Reports have yet to be independently verified

iPSC Teknolojisi

- İnsan kaynaklı pluripotent kök hücre (iPSC) teknolojisi, 2007'deki üretildiğinden bu yana hızla gelişti.
- İnsan iPSC teknolojisi hastalık modellemesi için yaygın olarak kullanılmaktadır; örneğin, nörodejeneratif ve psikiyatrik bozukluklar .
- İnsan iPSC teknolojisi şu anda klinik deneylerde kullanılarak birkaç ilaç adayı üretilmesine neden olmuştur.
- The first clinical trial using human iPSC-derived products has been initiated for age-related macular degeneration.

iPSC Technology

- Gen düzenleme ve 3B organoid teknolojileri ile birlikte iPSC teknolojisi daha güçlü olmuştur.

- İPSC teknolojisinin diğer teknolojilerle entegrasyonu ile sürekli gelişmektedir

iPSC Technology

- Kök hücre biyolojisi alanında
- Rejeneratif tıp alanında ,
- Hastalık modellemesi alanında
- İlaç keşfi alanında.
- Hastaya özel iPSC'leri kullanarak kişiye özel ilaç geliştirilmektedir.