Nuove frontiere dell'ingegneria tissutale in biomedicina

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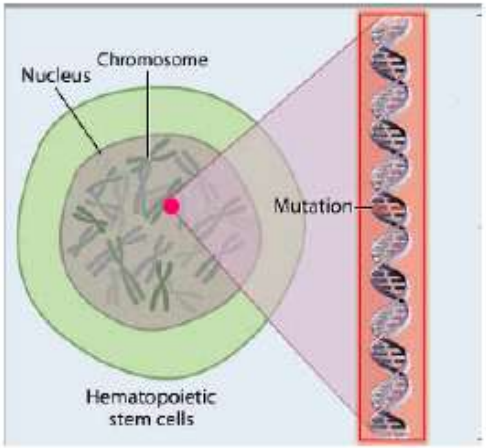
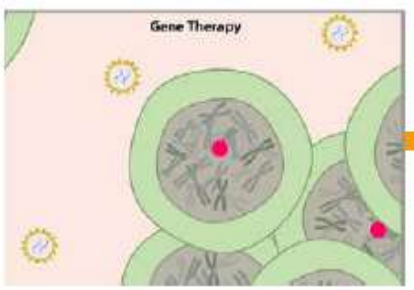
Outline

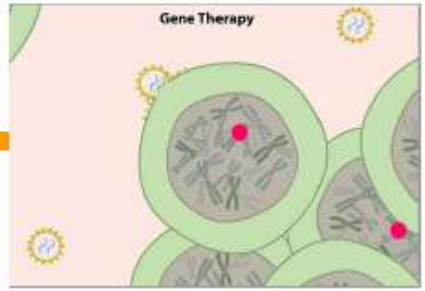
1. Modificazione dell'informazione genetica
2. Espansione controllata e guidata di cellule
3. Generazione di cellule staminali pluripotenti

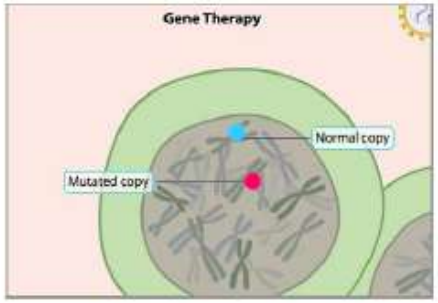
1. Modificazione dell'informazione genetica

Metodo tradizionale: sostituzione gene difettivo con uno funzionante



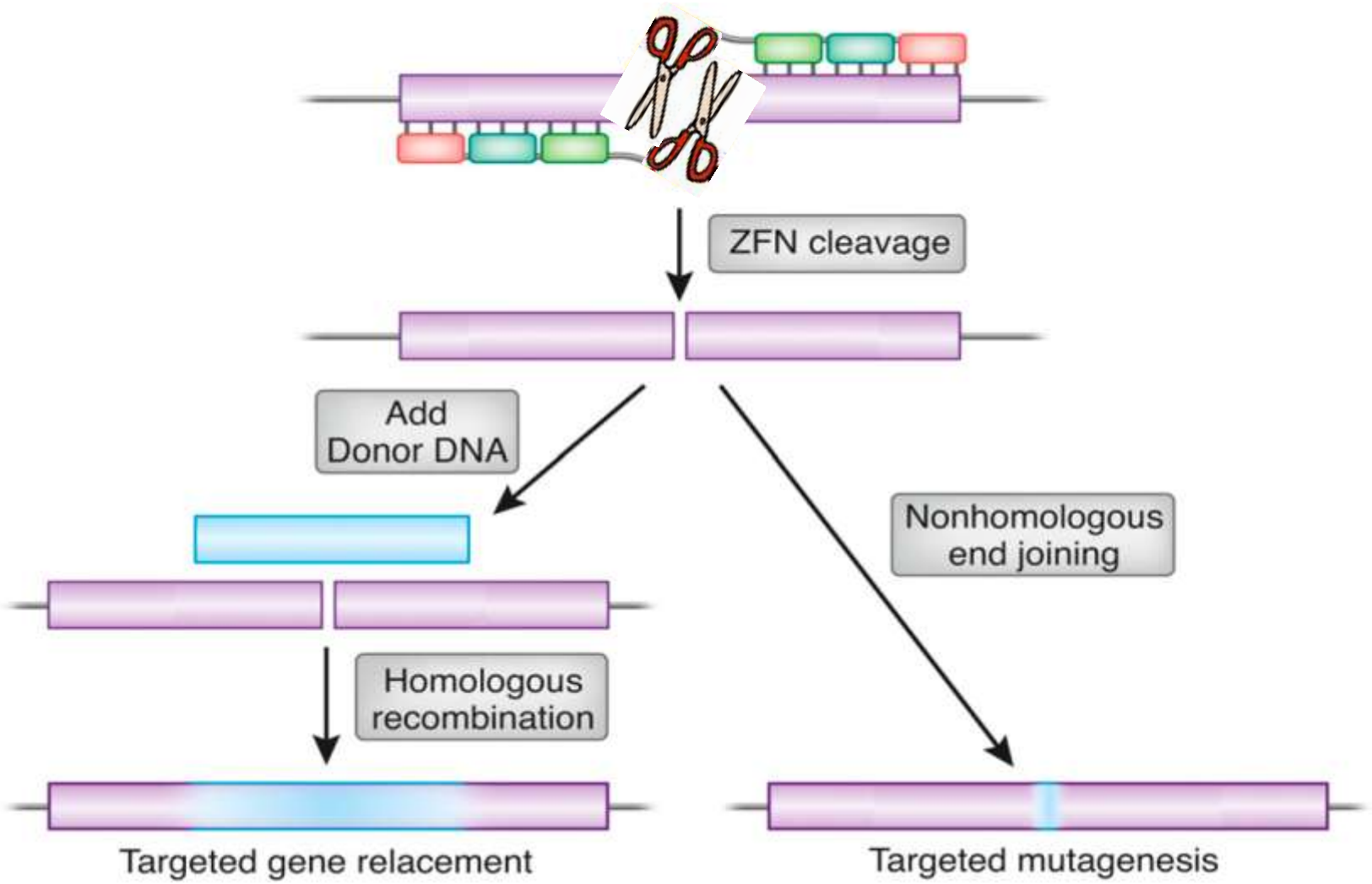






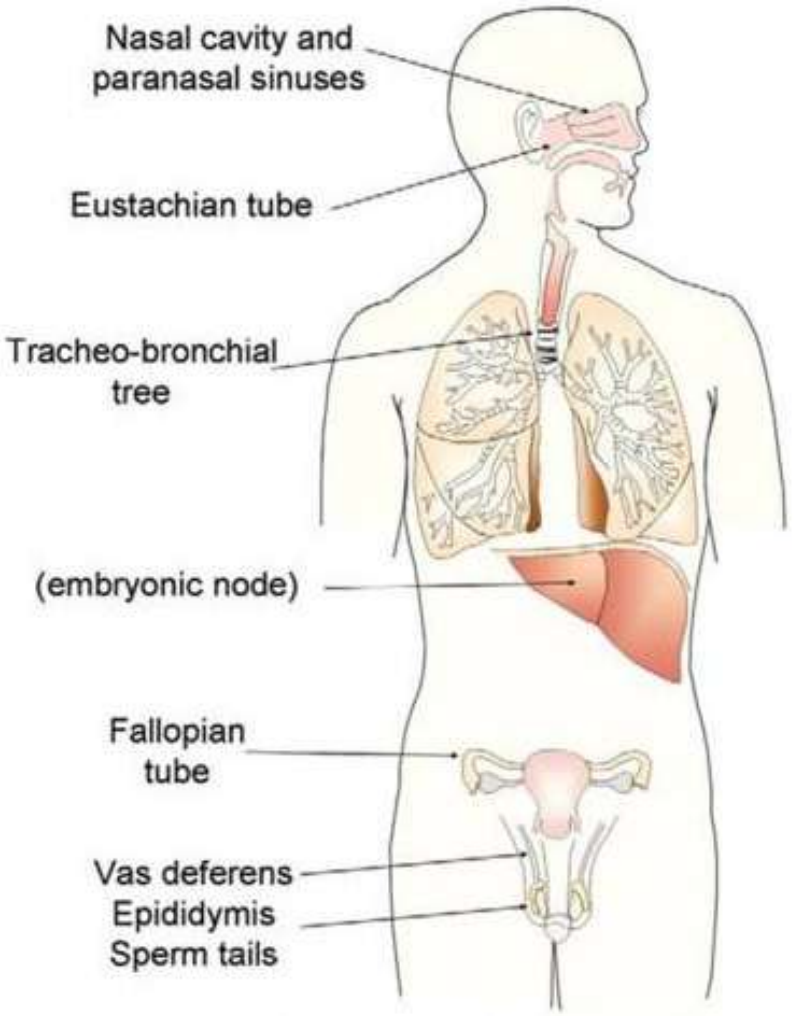
1. Modificazione dell'informazione genetica

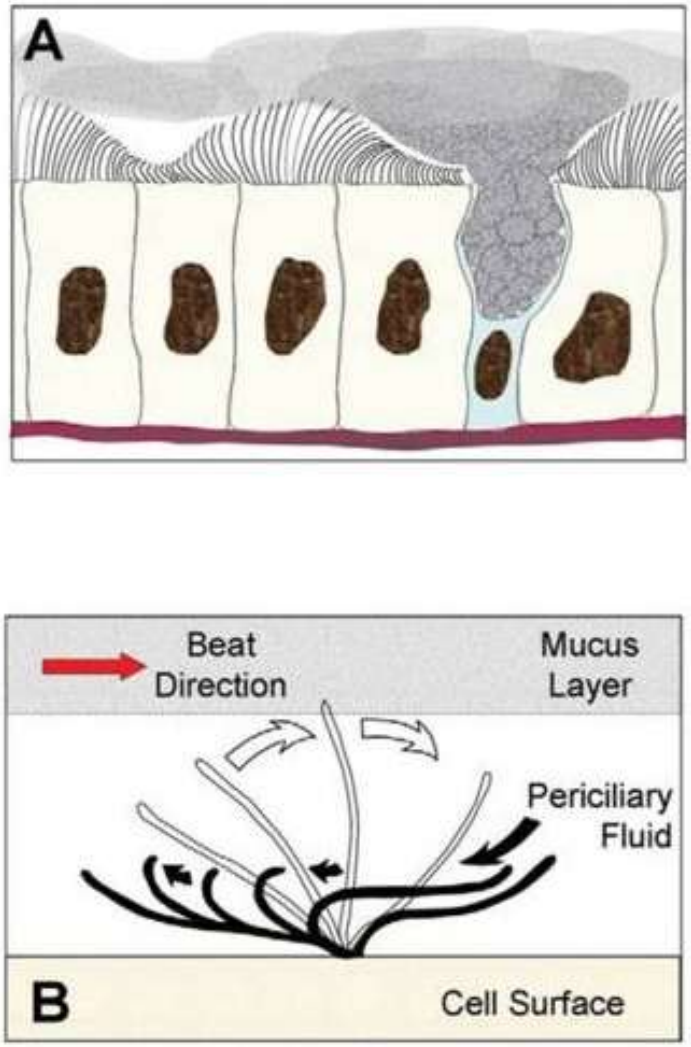
Nuovo approccio: *gene editing*



1. Modificazione dell'informazione genetica

Gene editing nella cura della discinesia ciliare primitiva





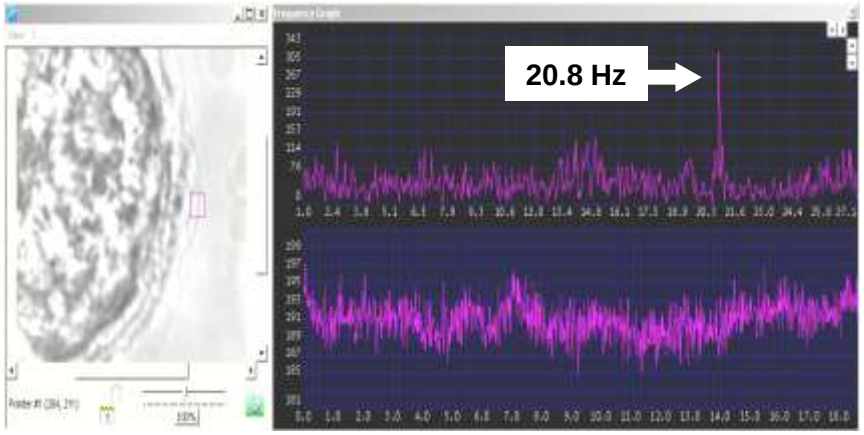
Rutland et al., Respiratory Ciliary Dysfunction, *in* Pediatric Respiratory Medicine 2nd ed., Taussig and Landau Eds., Mosby-Elsevier

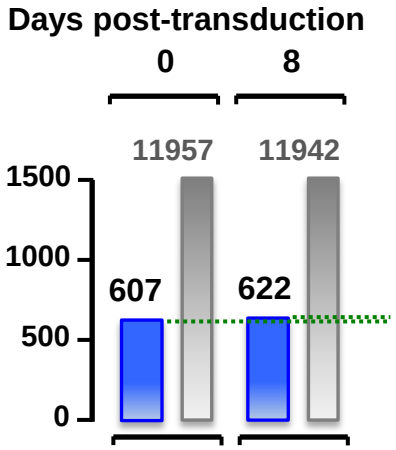
1. Modificazione dell'informazione genetica

Gene editing nella cura della discinesia ciliare primitiva

Combination /
Spheroids treated with

A /
Mock

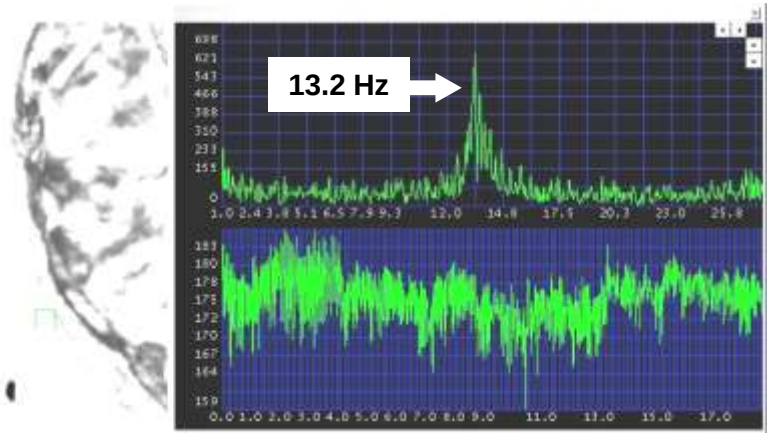


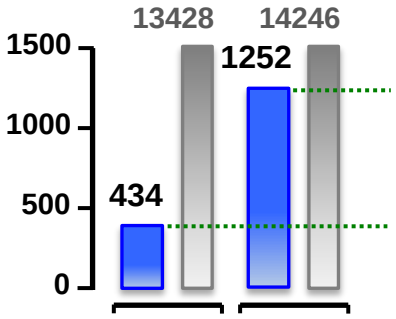


% increment of cells with wild-type sequence

0.012

C /
L- and R-TALENs
Rec





32.667*

Lai *et al*., AJRCCM 2014

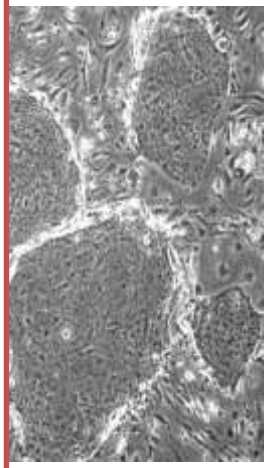
2. Espansione controllata e guidata di cellule

Background

In contrast to tumors, normal cells have limited life, proliferate until they reach the (Hayflick's) limit then senesce and die

Is it possible to immortalize cells AND maintain their normal properties?

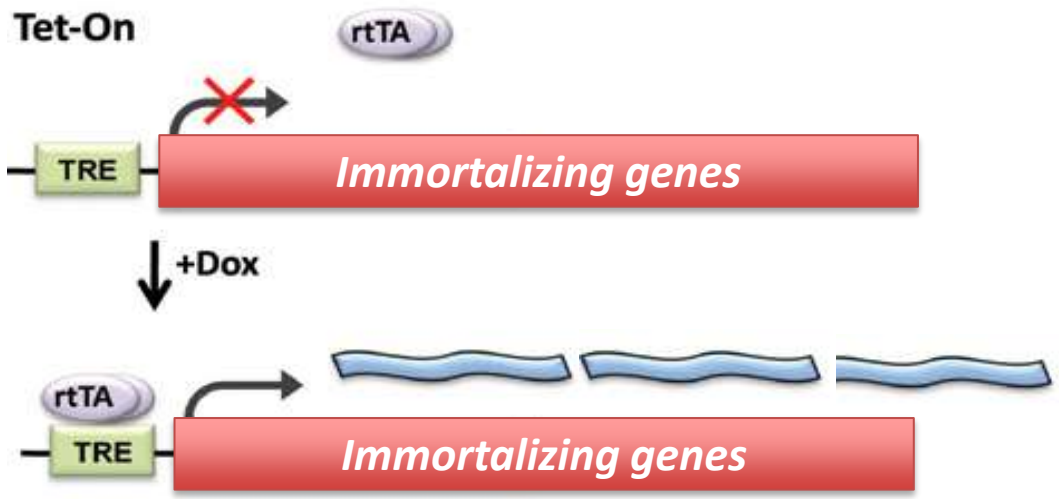
Standard approach: Irreversible transformation



, aneuploid and
aberrations

A novel, drug-inducible and fully reversable approach:

Ambrosia



VECTAGENE

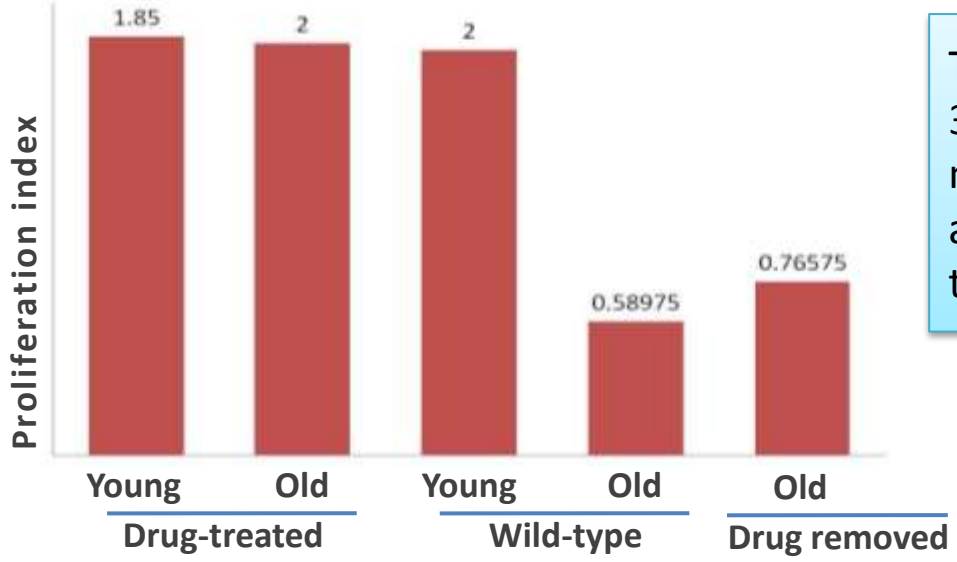
2. Espansione controllata e guidata di cellule

Human fibroblasts

No drug

Drug-treated ***(4 days)***

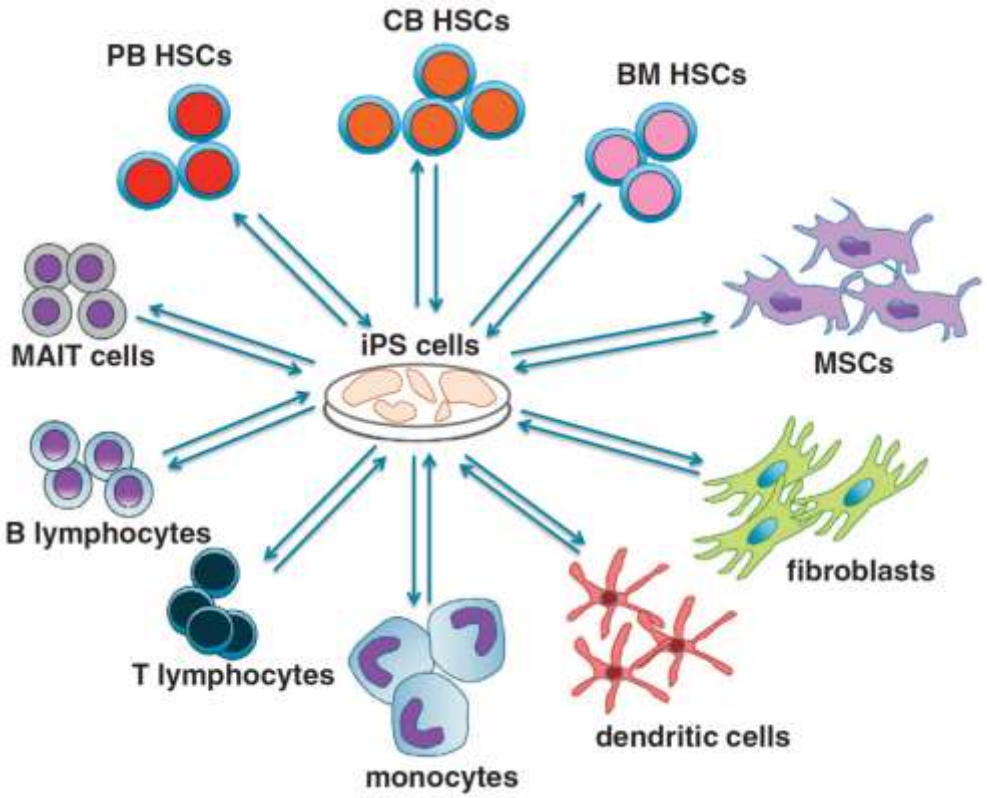
Drug removed ***(2 days)***



The DNA methylation pattern of 38 tumor suppression genes did not change after drug-treatment and was found identical to wild-type cells

VECTAGENE

3. Generazione di cellule staminali pluripotenti



Generation of totipotent stem cells

Oocyte

Fertilization

sperm cell

Fertilized oocyte

Embryonic stem cells (ESC)

Generation of totipotent stem cells

Somatic cell

Treatment with

OCT4 + SOX2 + KLF4 + c-*myc*

Induced pluripotent stem cells (iPSC)

(Takahashi, Cell, 2006)

Focosi et al., Blood Cancer Journal (2014) 4, e211