Sleeping Beauty Mediated Transposition in Hematopoietic Stem Cells

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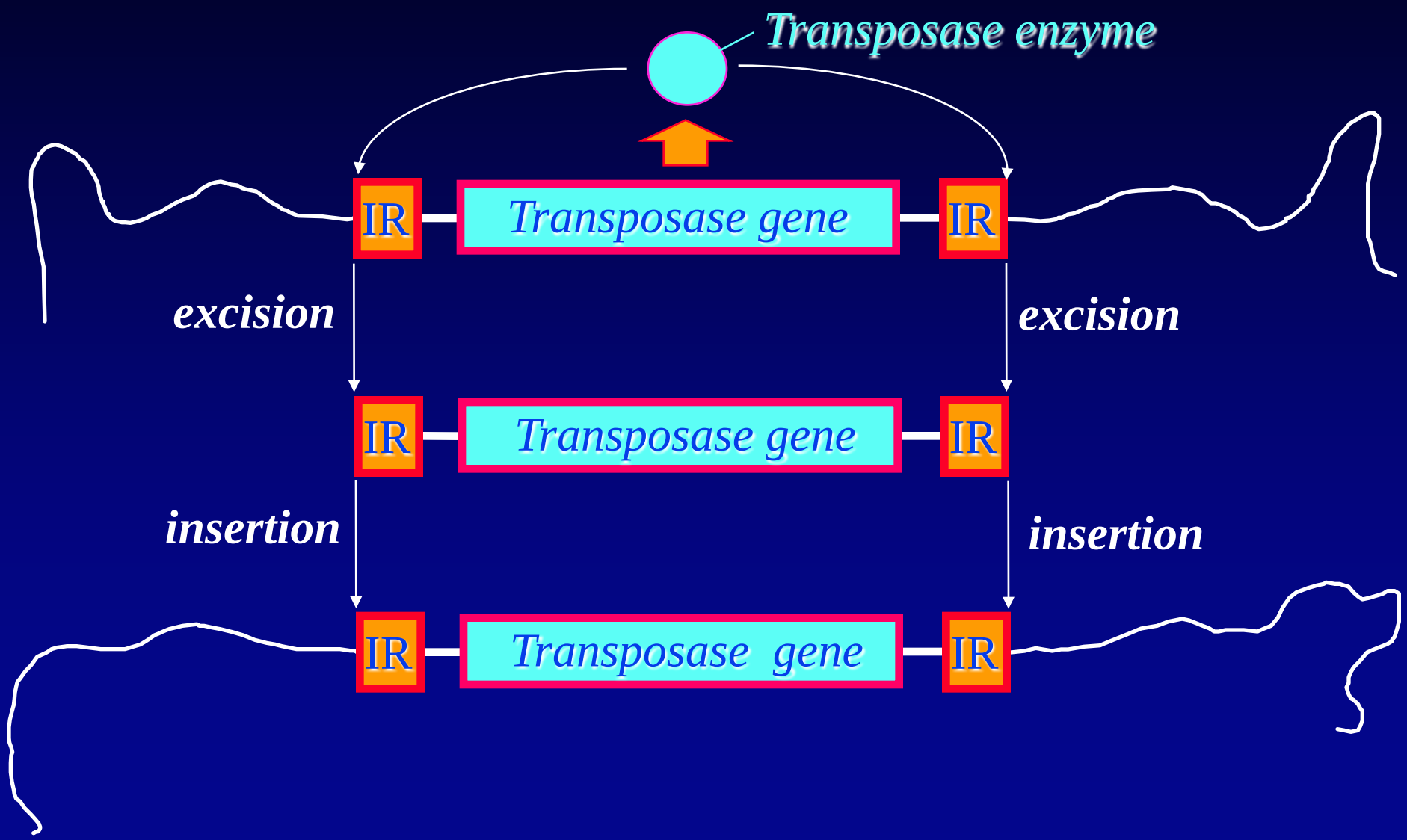
- **Potential Advantages of Transposons for Gene Therapy**
- ***Sleeping Beauty* Mediated Gene Transfer into Hematopoietic Stem Cells**
- **Site-Directed Transposition**

Cut-and-Paste Mechanism of Transposition



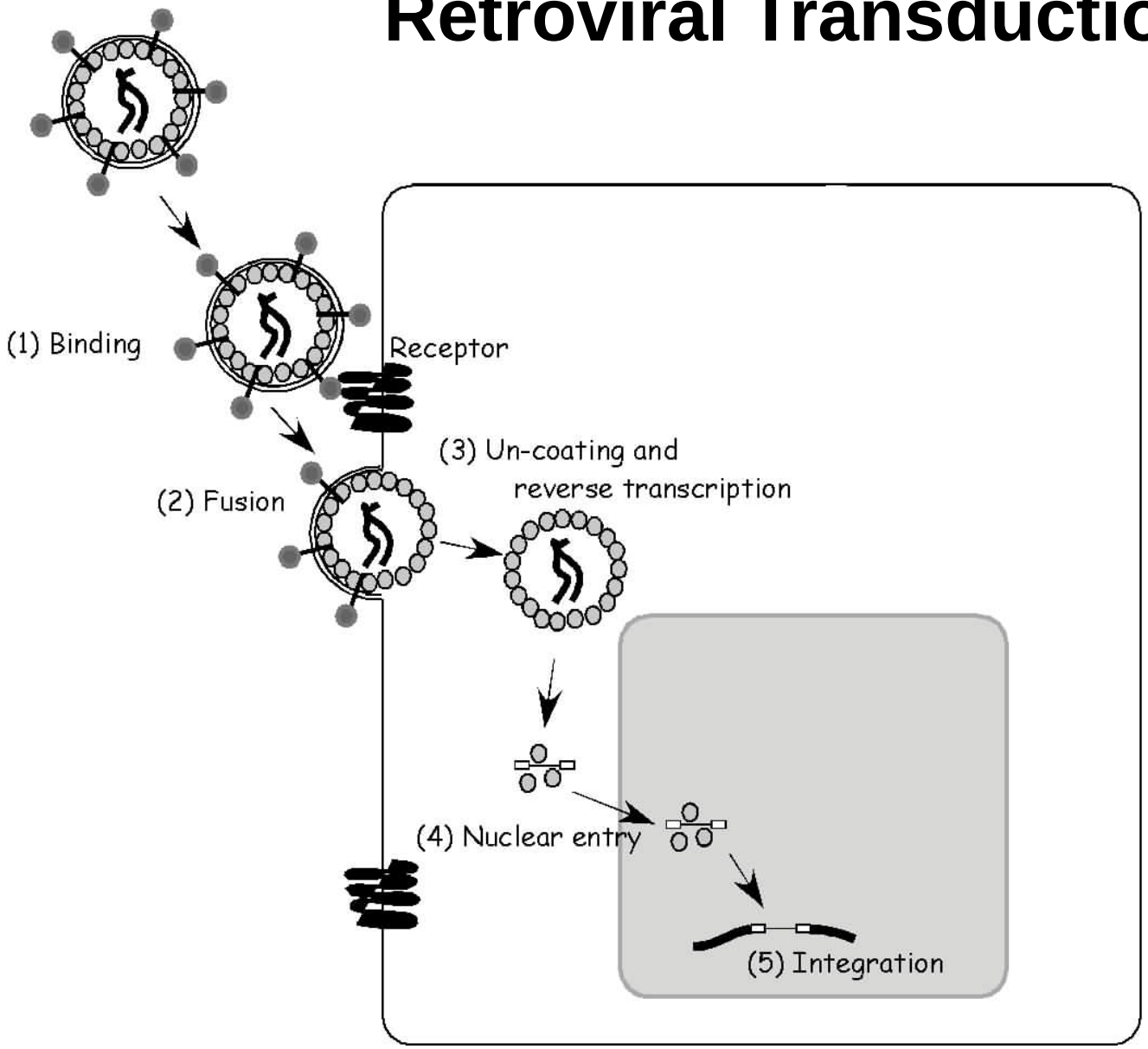
Recombinase Mediated Gene Transfer

- *Sleeping Beauty* Transposon
- ϕC31 Integrase
- PiggyBac Transposon
- Tol2 Transposon

SB Mediated Gene Transfer: Potential Advantages

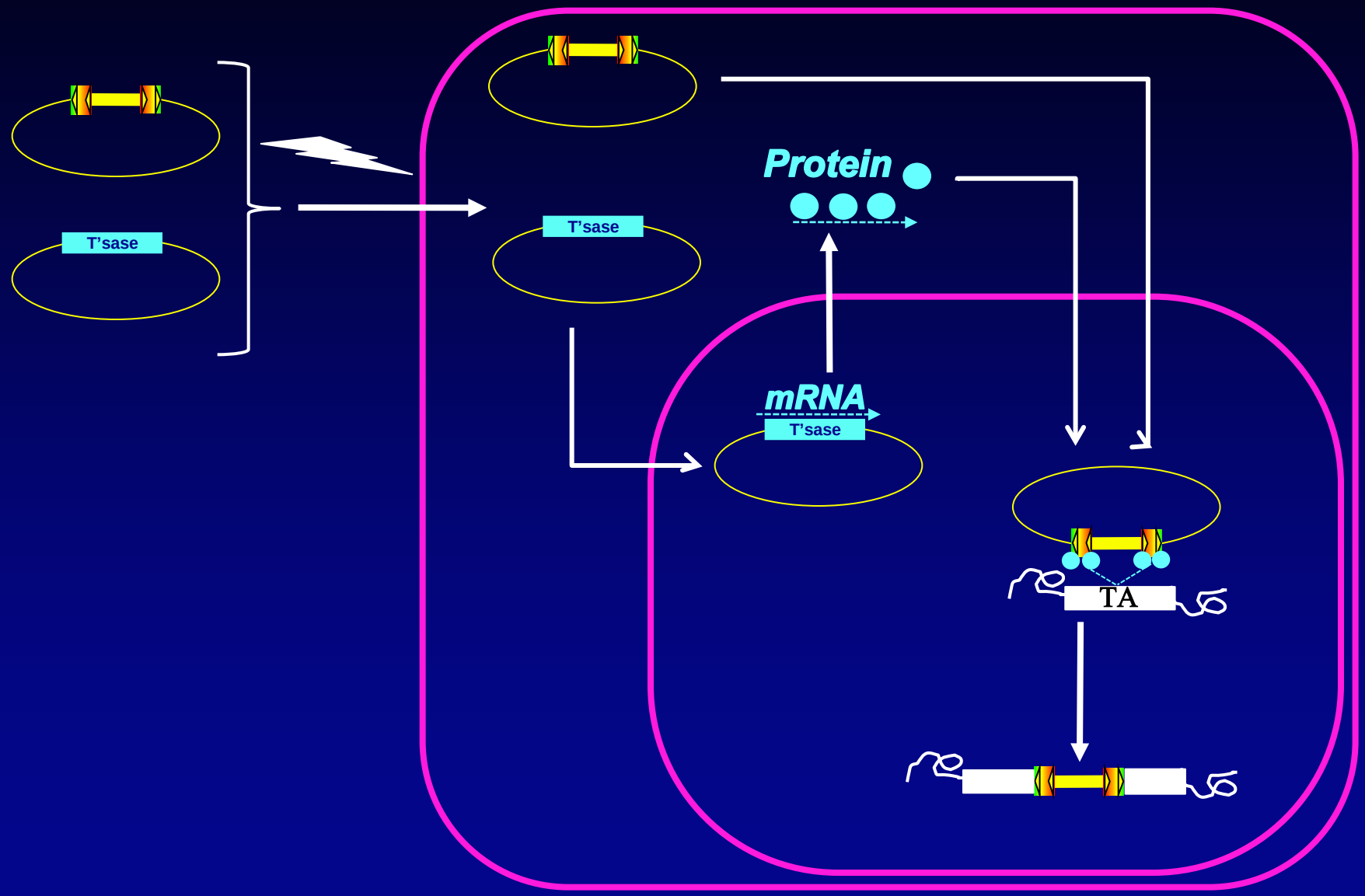
- Manufacturing straightforward
- More cost effective
- Less risk of biological contaminants
- Less risky integrant profile

Retroviral Transduction



Nik Somia

Sleeping Beauty Mediated Gene Transfer



Sleeping Beauty Mediated Gene Therapy in Models of Human Disease

- Hemophilia B (Yant *et al* Nat Genet '00)
- Hereditary Tyrosinemia (Montini *et al* Mol Ther '02)
- Junctional Epidermolysis Bullosa (Ortiz-Urda *et al*, Gene Ther '03)
- Hemophilia A (Ohlfest *et al*, Blood '05; Liu *et al*, Mol Ther '06)
- Mucopolysaccharidosis Type 1 (Aronovich *et al*, Mol Ther '07, Mol Ther '09)
- Glioma (Ohlfest *et al*, Mol Ther '05)
- Human T Cells (Huang *et al*, Blood '06)
- B Cell Leukemia (Huang *et al*, Mol Ther '07; Singh *et al*, Canc Res '08)

SB Mediated Gene Transfer in Human Cord Blood Hematopoietic Stem Cells

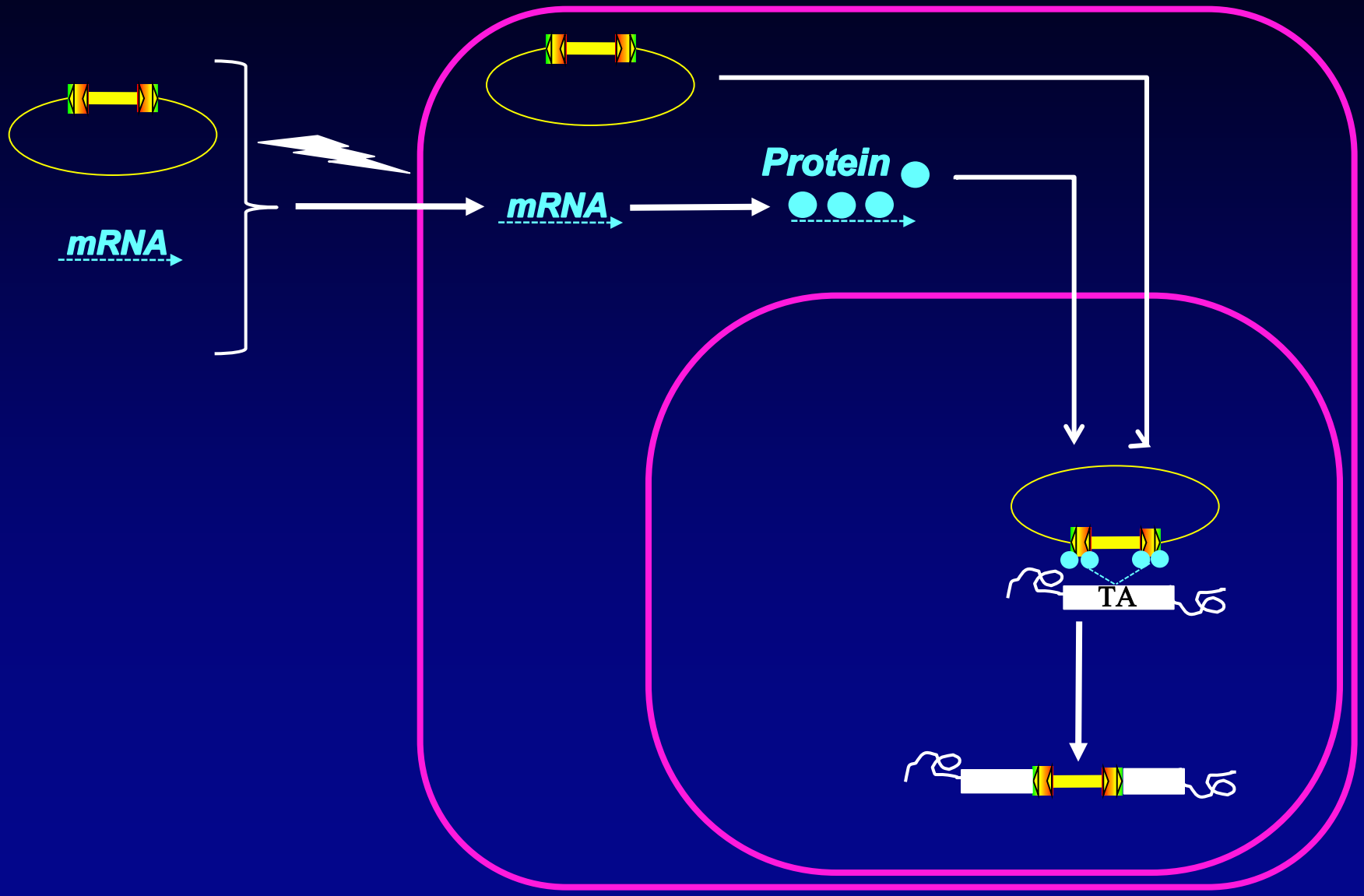
- Mates *et al*, Nat Genet ’09
- Xue *et al*, Blood ’09
- Sumiyoshi *et al*, Human Gene Therapy ’09

→ Therapeutic Gene Transfer
Into Hematopoietic Stem Cells

Sleeping Beauty Mediated Transposition in Human HSC: Future Challenges

- Therapeutic Gene Transfer into HSC
- Gene Transfer into Marrrow / Peripheral Blood Derived HSC
- Gene Transfer into Mouse HSC
- Protein or RNA as a Source of SB Transposase

Sleeping Beauty Mediated Gene Transfer



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