細胞治療產品
製程管控關鍵解析

日期 **2023.6.27**（二）

地點 台大醫院國際會議中心401室

指導單位｜ 衛生福利部　主辦單位｜ 財團法人醫藥品查驗中心

新穎間葉幹細胞平台

台寶生醫股份有限公司
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新穎間葉幹細胞平台

Taiwan Bio Therapeutics

27.06.2023

A brief history of MSC development

A rough path

- A not applicable success story of HSC transplantation
  - ✓Wrong MoA
  - ✓Limited in vivo knowledge
- A good safety profile with limited clinical efficacy
  - ✓Heterogeneity
  - ✓Limited stemness
- Multiple strategies being tested for efficacy improvement
  - ✓Primed
  - ✓Induction
  - ✓Gene engineering

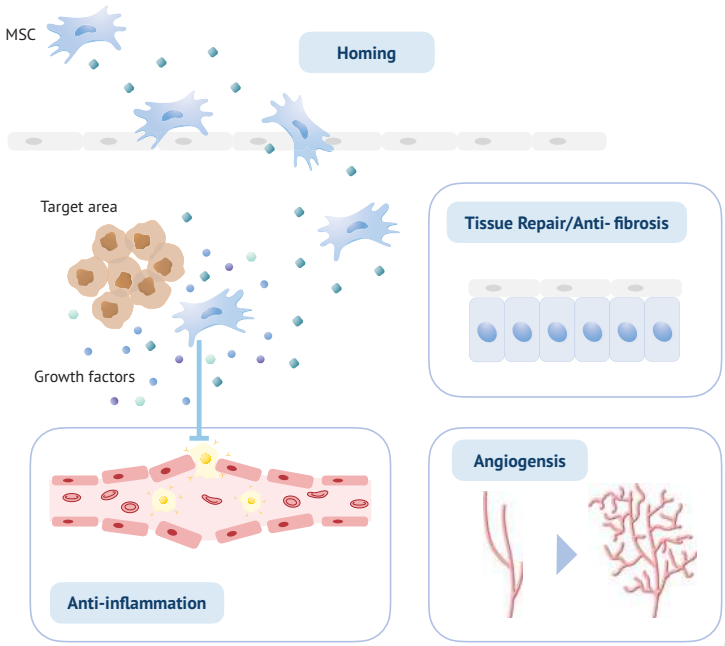
MSC: a safe, potent and allogeneic cell type

Mesenchymal stromal cells are multi-functional cells that can be used as allogeneic therapies

- Potent and multifunctional
  Promote tissue repair, anti-inflammatory, immune modulation and anti-fibrosis through **growth factor secretion**.
- Safe
  Not carcinogenic or tumourigenic, low risk of rejection due to low MHC class II expression. Clinical trials show excellent tolerability.

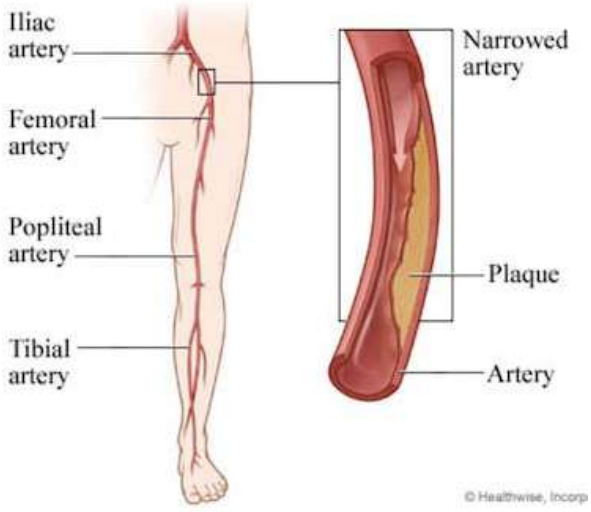
SuperCarrier MSC

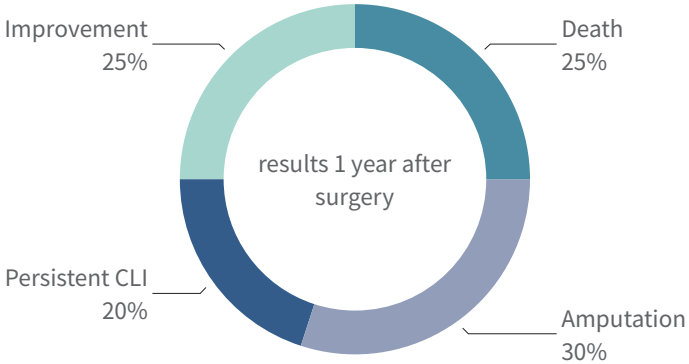
Through genetic engineering, increase the secretion of a selected growth factor or cytokine by >7-fold



Critical limb ischemia

The limb killers with huge unmet medical needs





MSC/VEGF- first in class and the best shot for therapeutic angiogenesis

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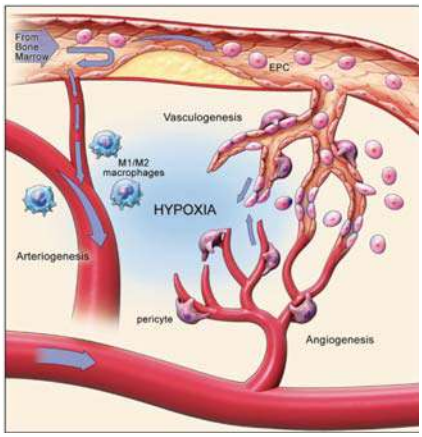
To be the first treatment targets critical limb ischemia to reduce amputation rates

Reference	Year	Disease	Gene	Delivery	Vector	No. of patients	Total dose	No. of doses
Phase I								
Isner *et al.*[15]	1996	CLI	VEGF	IA	Plasmid	1	2 mg	1
Baumgartner *et al.*[16]	1998	CLI	VEGF	IM	Plasmid	9	4 mg	2
Isner *et al.*[17]	1998	CLI	VEGF	IM	Plasmid	6	2–4 mg	2
Simovic *et al.*[18]	2001	CLI	VEGF	IM	Plasmid	29	3–9 mg	2–3
Shyu *et al.*[19]	2003	CLI	VEGF	IM	Plasmid	21	0·8–5·2 mg	2–3
Kim *et al.*[20]	2004	IC/CLI	VEGF	IM	Plasmid	9	2–8 mg	2
Rajagopalan *et al.*[21]	2001	IC/CLI	VEGF	IM	Virus	5	4×10^8 to 4×10^{10} units	1
Rajagopalan *et al.*[22]	2002	IC	VEGF	IM	Virus	18	4×10^8 to 4×10^{10} units	1
Comerota *et al.*[23]	2002	CLI	FGF	IM	Plasmid	51	0·5–16 mg	1
Rajagopalan *et al.*[24]	2007	CLI	HIF-1α	IM	Virus	34	1×10^8 to 2×10^{11} units	1
Morishita *et al.*[25]	2004	CLI	HGF	IM	Plasmid	6	4 mg	2
Phase II								
Mäkinen *et al.*[26]	2002	IC/CLI	VEGF	IA	Virus/plasmid	54	2 mg; 2×10^{10} units	1
Rajagopalan *et al.*[27]	2003	IC	VEGF	IM	Virus	105	4×10^9 to 4×10^{10} units	1
Kusumanto *et al.*[28]	2006	CLI	VEGF	IM	Plasmid	54	4 mg	2
Nikol *et al.*[29]	2008	CLI	FGF	IM	Plasmid	125	16 mg	4
Powell *et al.*[30]	2008	CLI	HGF	IM	Plasmid	104	1·2–12 mg	2–3
Grossman *et al.*[31]	2007	IC	Del-1	IM	Plasmid	105	42 mg	1
Phase III								
Belch *et al.*[32]	2011	CLI	FGF	IM	Plasmid	525	16 mg	4



- Multiple VEGF gene therapy trials and MSC trials showed limited efficacy
- We used MSC as a vehicle to achieve high local VEGF concentration
- MSC/VEGF maintains features of MSC, and has potential to create and maintain new vasculature

Therapeutic angiogenesis

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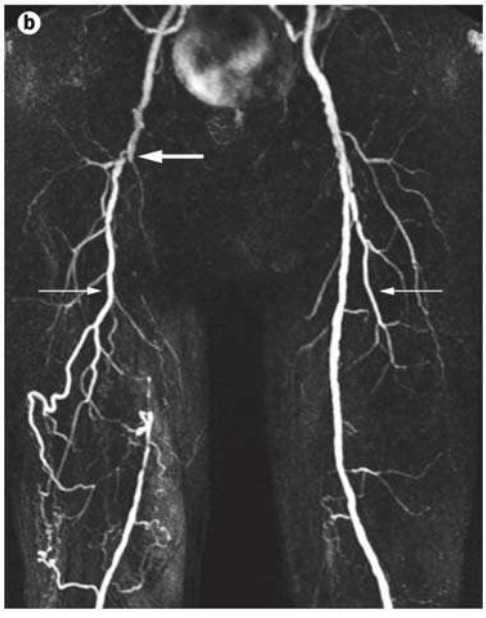
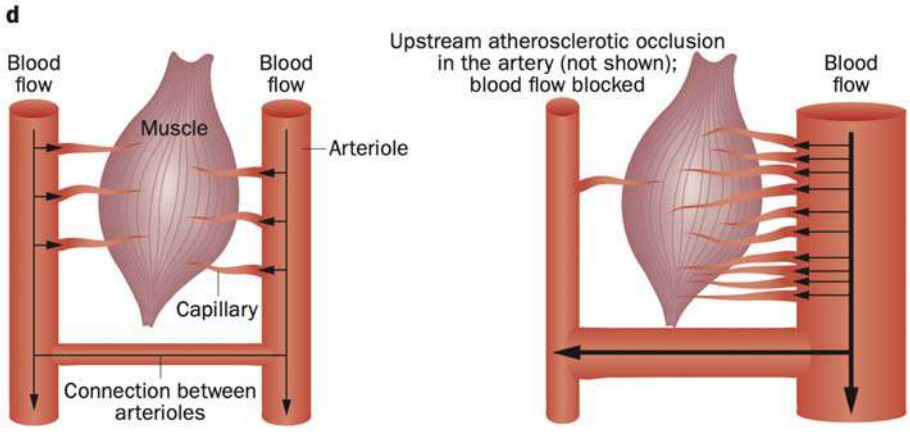
Generating and maintaining new blood vessels from existing vasculature





Platform technology

a group of technologies that are used as a base upon which other applications, processes or technologies are developed.

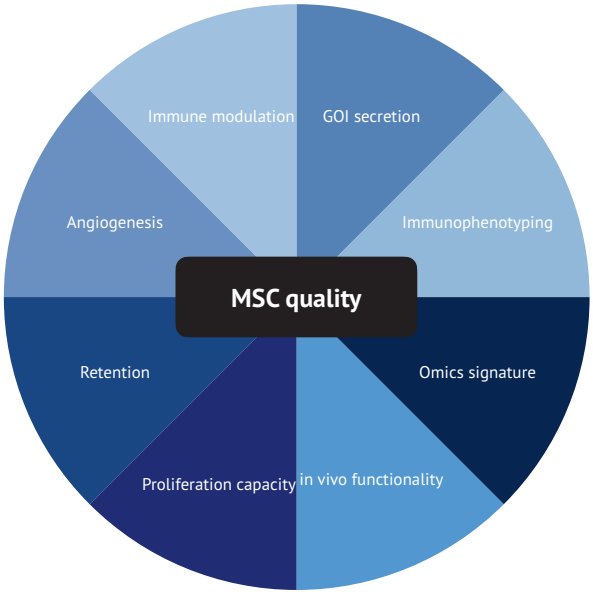
Our SuperCarrier MSC engineering platform

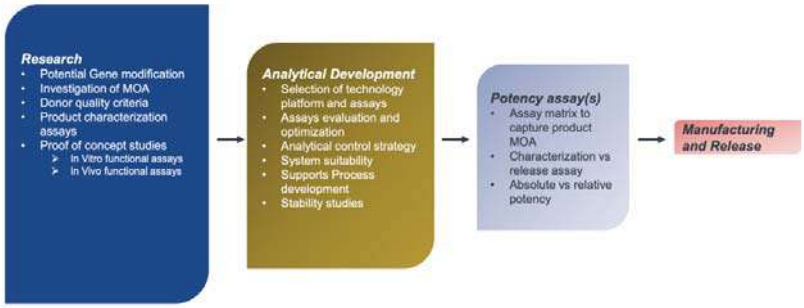
Payload, characterisation and manufacturing

- Payload design (GOI)
- Transduction vector
- Cell characterisation
- Assay development
- Process design
- Process automation

Why we need a platform?

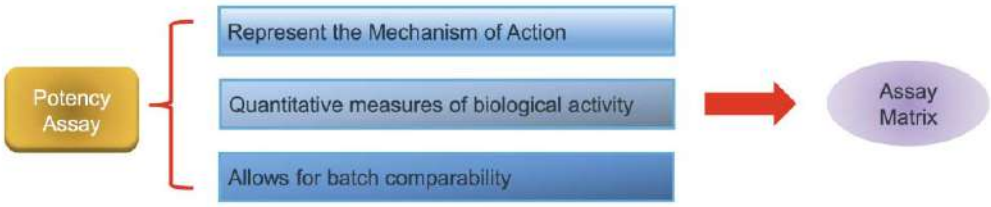
To capture the complexity of cell functionality





Why potency matters?

No potency, no BLA

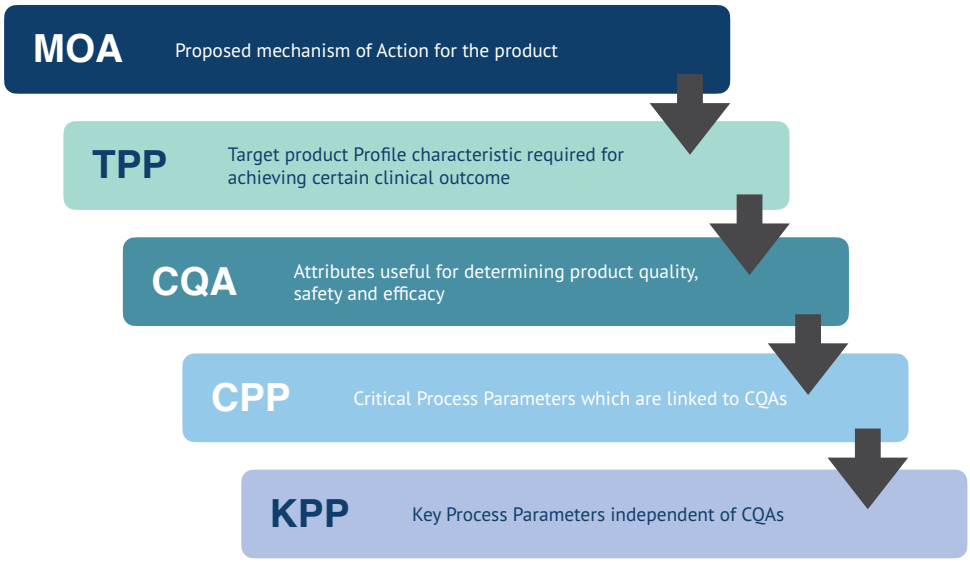


- Potency is defined as "the specific ability or capacity of the product, as indicated by appropriate laboratory tests or by adequately controlled clinical data obtained through the administration of the product in the manner intended, to effect a given result." (21 CFR 600.3(s)). Strength6 is defined as "[t]he potency, that is, the therapeutic activity of the drug product as indicated by appropriate laboratory tests or by adequately developed and controlled clinical data. . . ." (21 CFR 210.3(b)(16)). Regulations require that "[t]ests for potency shall consist of either in vitro or in vivo tests, or both, which have been specifically designed for each product so as to indicate its potency in a manner adequate to satisfy the interpretation of potency given by the definition in § 600.3(s) of this chapter." (21 CFR 610.10).
- Potency tests, along with a number of other tests, are performed as part of product conformance testing,7 comparability studies (Ref. 3), and stability testing (Ref. 4). These tests are used to measure product attributes associated with product quality and manufacturing controls, and are performed to assure identity, purity, strength (potency), and stability of products used during all phases of clinical study. Similarly, potency measurements are used to demonstrate that only product lots that meet defined specifications or acceptance criteria are administered during all phases of clinical investigation and following market approval.

Our approach: rational cell therapy design

Define CQAs as early as possible

- characterising CQAs early
- develop fit-for-purpose assays to measure CQAs
- define CPP and preparing clients for future process optimisation
- transition from manual manufacturing processes to automation
- secure relevant materials and ensure their steady supply
- ensure the production process complies with regulatory requirements



Version. 2023

Thank you for your attention

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主辦單位｜財團法人醫藥品查驗中心