Data in support of the clinical use of adipose derived MSC: growth, storage, function and safety

Allan B. Dietz, Ph.D.

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Disclosures

A.B. Dietz is an inventor of technology described in this talk. The invention was licensed to Mill Creek Life Sciences, LLC, Rochester, MN. A.B. Dietz is a shareholder and Director of Mill Creek Life Sciences, Rochester, MN.
Adipose derived MSC

• Fat
  • Easy access
  • Less painful
  • Plenty of it

• Cell isolation method
  • Small biopsy
  • Brief digestion
  • Plating (Advance MEM; 5% PLTmax; Mill Creek life sciences)
Cells grow fast…
Independent of underlying disease/condition

- ALS
- MSA
- CLI
- Cancer
- Renal stenosis
- Obese
- Old
- Chron’s disease
You can freeze them up to one year, recover them and inject them ...
Functional…

- **Mature Dendritic Cells (percent CD83+)**
  - Control
  - MSC
  - Dex
  - p<0.001
  - p=0.03

- **CD4+ eFluor670low (Percent)**
  - T cells: Allogeneic DC ratio
  - 5:1
  - 10:1
  - *

- **MSC Inhibition of T cell proliferation in simulated GVH**
  - 5:1
  - 10:1
Safety

- Tumor formation (malignant transformation)
- Migration (targeted effect)
- Route of delivery
- Context of condition
  - (is it safe in the indication specified?)
Safety – Tumor formation

- Malignant transformation
- IF malignant transformation occurs – likely that it will happen in later doublings AND – will grow in vivo

- >25 population doublings; >1 trillion (x10^{12} cells from our typical culture)
- 3 preps; 9 mice (SCID) for each prep
- Flank (6 mice at 20E6) or IP (3 mice at 40E6; 140 billion HE)
- Control is 5E6 SKOV
Safety – Tumor Formation - SubQ

No tumor or mass visible or palpable.

Site of subcutaneous injection has no appearance of cells seeding or growth.
Safety – Tumor Formation - IP

Masson-Trichrome staining
Black = nuclei
Purple/Red = cytoplasm & muscle fibers
Blue = collagen

No tumor – did form adhesions - collagen at very high injection numbers
Safety – Intrathecal injection

- Large animal model for route of injection and biodistribution safety
- Intrathecal injection of autologous MSC
  - 10E6; 19 animals
  - 10E6; 10 animals X 3 injections
  - 3 deaths (injection site trauma)

Complete autopsy
All major organ pathology
Behavior
Biometrics: weight monitoring

Normal Pathology; normal behavior
Safety – Intra-renal injection

• Large animal model for route of injection and bio-distribution safety in disease model and healthy swing

• Intra-renal injection of autologous MSC

• 2-7.510E5 cells/kg

• 17 swine/some stenotic models

 Complete autopsy

 All major organ pathology

 Biometrics: weight monitoring

Normal Pathology; normal behavior; 4-14% of cells remain in organ; signs of improved function
MSC for Renal Stenosis

Normal  Diseased  Diseased + MSC
Conclusions

• adMSC
  • Grow rapidly
  • Consistent growth from multiple diseases
  • Freeze deliver well
  • Immune suppressive/capable of differentiation

• Safety of adMSC
  • Late doublings/massive injection in immune deficient mice – no tumors
  • Eight animal studies; >70 animals; three species

PREDICTIBLE, FUNCTIONAL AND SAFE
Thanks

Missing: Dennis Gastineau, M.D.