

זכורו ח' ג-ה: פה אמר ה' שְׁבַתִּי אֶל צִוָּן וְשִׁכְנַתִּי בְּתוֹךְ יְרוּשָׁלָם...

וַרְחֲבוֹת הָעִיר יִמְלָאוּ יְלִדִים וַיְלִדוֹת מִשְׁתְּקִים בְּרַחֲבָתָה.



תמונות הקשת האוטיסטית וטיפול בתאי גזע: כיוון חדש ומבטיח

AUTISM SPECTRUM DISORDERS AND STEM CELL THERAPIES: A PROMISING NEW DIRECTION

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ASD = Autism *Spectrum* Disorder



Diagnostic

Therapeutic



Contents lists available at SciVerse ScienceDirect

Journal of Autoimmunity 2013

journal homepage: www.elsevier.com/locate/jautimm

Review

Immunological and autoimmune considerations of Autism Spectrum Disorders

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Marion Leboyer^u, Dominique Farge-Bancel^v, Paul Ashwood^{w,x}

IF 7.641

Quoted in >100 papers

3



Witebsky-Rose Criteria for Auto-Immune Disease

A. DIRECT PROOF

Non-pathogenic maternal antibodies may produce disease in infant



1. Presence of Non-pathogenic IgG antibodies

- *NO clinical effect in adults*
- **Autoimmune disease ± family history of ASD**
("Circumstantial Evidence")

2. During Pregnancy – maternal IgG antibodies

- **Effect on Fetal Brain Development**

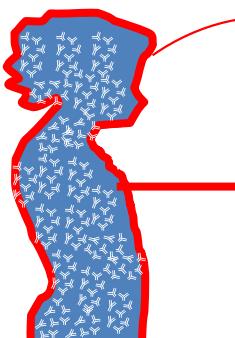
3. Postnatally:

- *Child presents clinically with features of ASD*
- *Maternal antibodies in child with ASD*

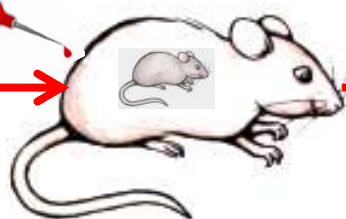


4. Maternal antibodies injected to pregnant mouse

Braunschweig *et al.* Maternal autism-associated IgG antibodies delay development and produce anxiety in a mouse gestational transfer model.
J Neuroimmunology 252 (2012) 56–65



Pregnant mouse

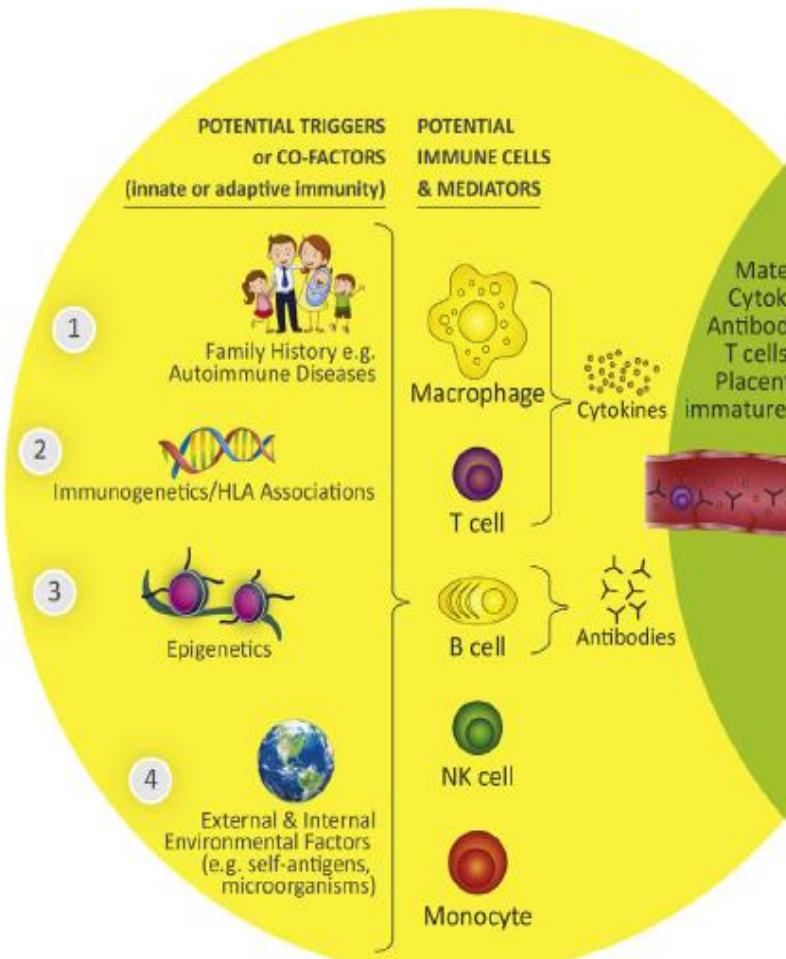


Autistic Features in Offspring

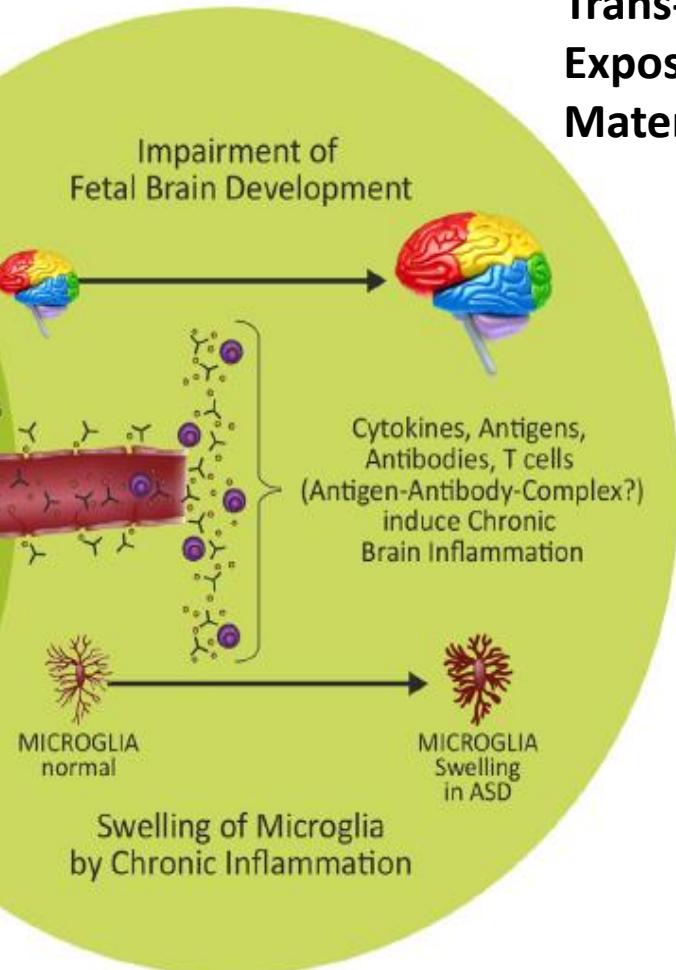


Immunology in the Pathogenesis of Autism

Maternal Immune System



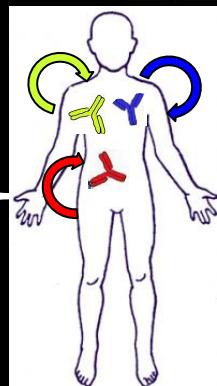
Fetal Nervous System



**Intra-uterine and/or
Trans-placental
Exposure to
Maternal Antibody**

D

Hypothesis: Autism has Auto-Immune Aspects Laboratory Diagnosis early in life (→ Treatment)



New Diagnostic
→ Therapeutic Strategies



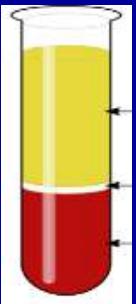
AAA = A_{uto-Immunity} A_{sso}ciated A_{utism}

- ✓ Routine blood sample collection for lab analysis

Cell EI's Preliminary Findings

ASD (>100)

TD (>50)



±1,000 Biomarkers in Serum

>20 Immunological Markers

→ Early Laboratory Diagnosis → Monitoring

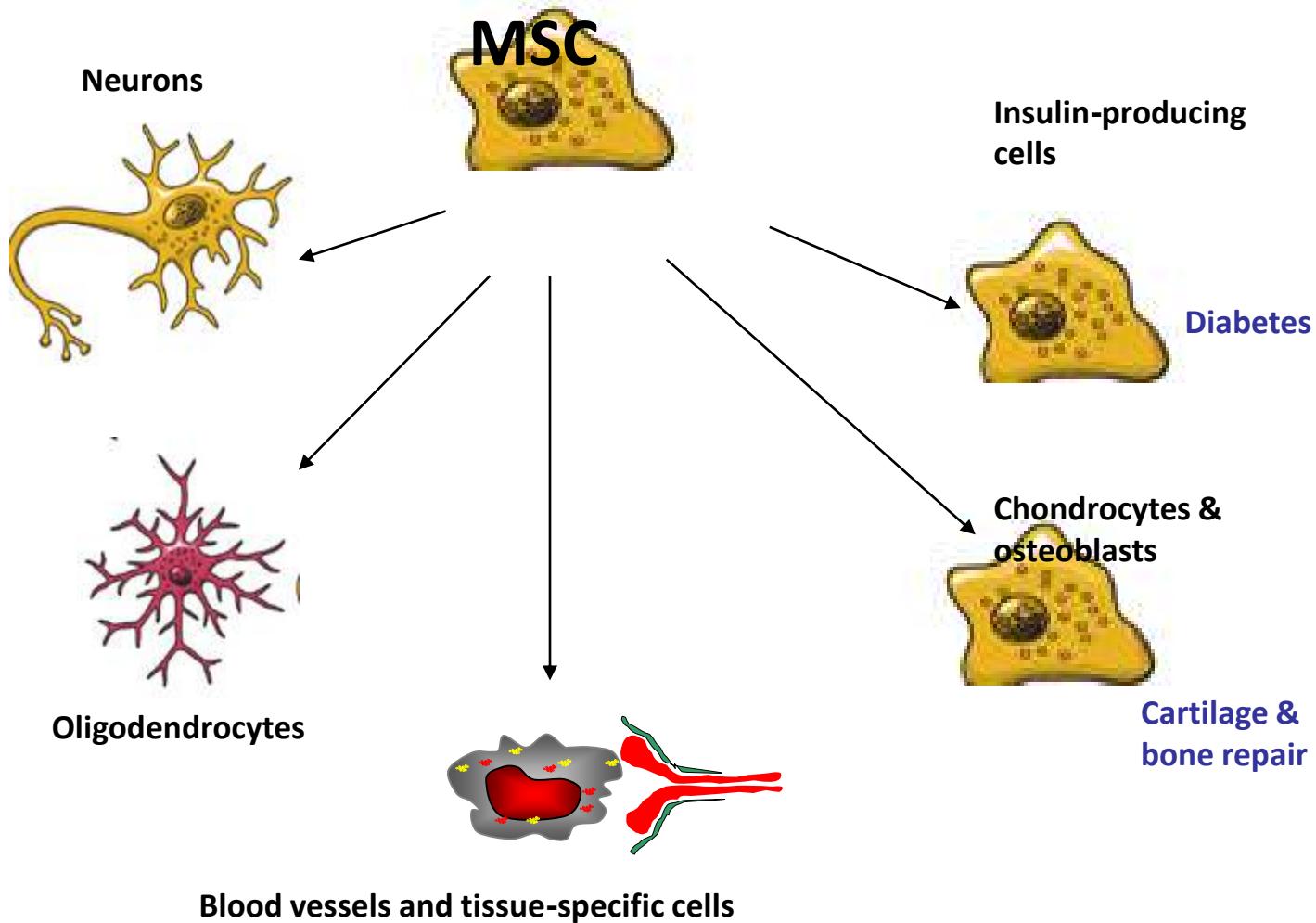
Clinical Research of bone marrow-derived MSCs: Neurogenesis, Regenerative Medicine

Neurodegenerative
Parkinson's Disease
Alzheimer's disease
ALS
Huntington's Disease

Spinal cord injury
Stroke (CVA)
HIE

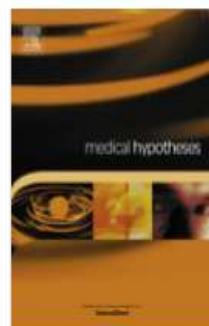
Autism?

Multiple sclerosis
Demyelinating
diseases of the CNS
and PNS



Contents lists available at [ScienceDirect](#)

Medical Hypotheses

journal homepage: www.elsevier.com/locate/mehy

Therapeutic properties of mesenchymal stem cells for autism spectrum disorders



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Therapeutic Rationale of MSCs for ASD

- Chronic autoimmune reactivity
- Neurogenesis \downarrow (*neuro-developmental disorder*)

Autism

**Patho-
genesis
of ASD
(?)**

- *Auto-immune process*
- *Neuro-genesis \downarrow*

MSC

**Biological
Properties
of MSC**

- *Immune modulation*
- *Neuro-genesis \uparrow*

MSCs suppress immune dysfunction while promoting neurogenesis → MSCs may be appropriate therapy for ASD in young children.

Synergistic Effect (1 + 1 \geq 2)



Autologous source of MSC

- Patient's own cells (might be affected by disease)
- No immune reactions
- Bone marrow aspiration & sedation required
- Laboratory work necessary for each patient
- Procedure dependent treatment
- Expensive and time consuming

Allogeneic source of MSC

- From healthy & young individuals
- Potential immune reaction
- No need for procedure and laboratory work (for commercial MSCs)
- Cellular treatment is clinically ready to go
- Opportunity for patentability

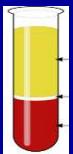
Gesundheit, B et al: Therapeutic properties of mesenchymal stem cells for autism spectrum disorders. Med Hypotheses. 2015 Mar;84(3):169-77.

Dawson, G et al. Autologous Cord Blood Infusions are Safe and Feasible in Young Children with Autism Spectrum Disorder: Results of a Single-Center Phase I Open-Label Trial. Stem Cells Transl Med. 2017 May;6(5):1332-1339.

Treatment with Bone Marrow-Derived Stem Cells (BM-SC)

1. Evaluation

- Clinical,
Psychological
- Laboratory
(serum, stool ,
urine)

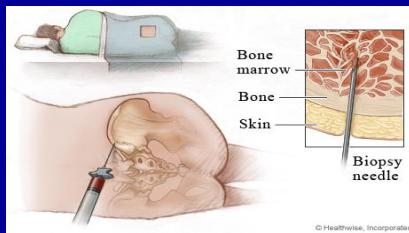


<1 month

Pre-treatment

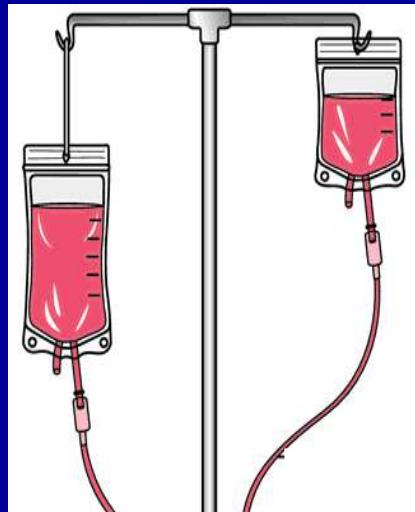
2. Bone Marrow Aspiration

(3-5 mL/kg body weight) →
separated in Operating Room



3. Administration

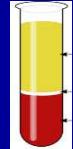
IV + IT



Mild sedation, < 1 hour, ambulatory

4. Evaluation

- Clinical,
Psychological
- Laboratory
- serum, stool,
urine)



1 + 3 + 6 months

post-treatment

Treatment with Bone Marrow Derived Stem Cells (BM-SC)

1. Evaluation

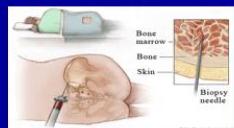
- Clinical (ADOS...)
- Laboratory (serum, stool & urine)



<1 month
pretreatment

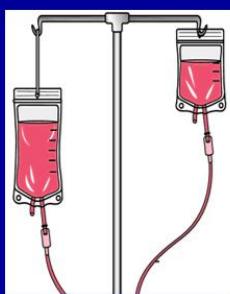
2. Bone Marrow Aspiration

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3. Administration

IV + IT



Mild sedation, < 1 hour, ambulatory

4. Evaluation

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- Laboratory (serum, stool & urine)



1 + 3 + 6 months
posttreatment



www.Cell-El.com

Cell El's Preliminary Clinical Experience



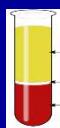
Pre-Treatment Post-Treatment

Comments

#1	<u>ATEC</u>	63	23	Uses I/me, friendships
	<u>SCQ</u>	23	13	Language↑



#2	<u>SCQ</u>	19	13	Attention span ↑ Social skills ↑
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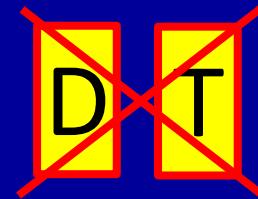


Serum,
Urine,
stool...

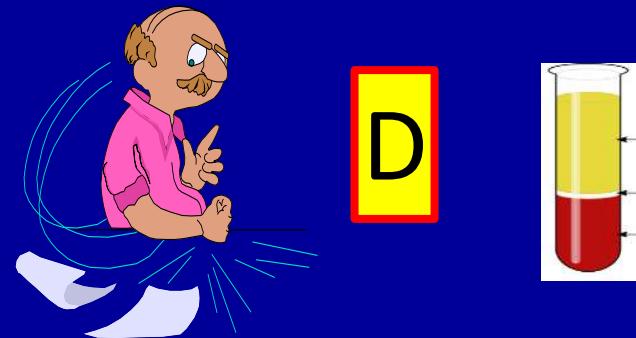


SUMMARY & CONCLUSIONS

- ASD = Autism *Spectrum* Disorder →
(no biological diagnosis)



- Diagnostic Immune Markers



- Therapeutic Effects from autologous Stem Cells



TEAMWORK makes the DREAM WORK



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Ron Ellis
PhD MBA, CTO



**Baruch
Labinsky** CBO



**Philip
Zisman** PhD



**Yehudit
Posen** PhD



**Leah
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**Susan
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