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Topical Agents: cell therapies and tissue engineering products

ASP workshop
February 21, 2014

Nasreen Jacobson
Vincent Ronfard

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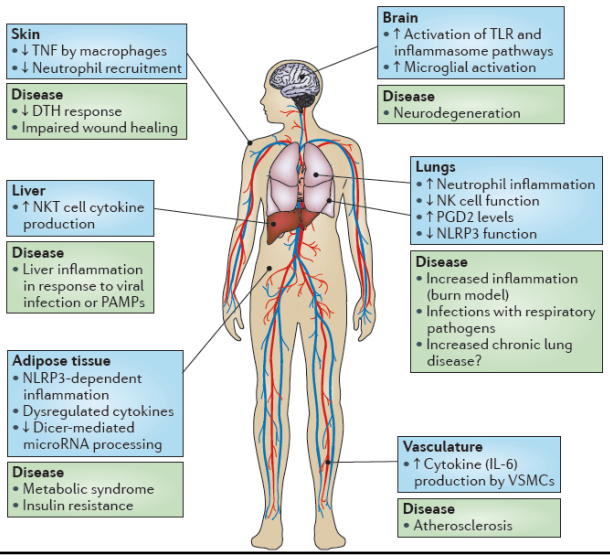
Factors affected during aging impact normal wound healing



- Altered Inflammatory response
- Altered chemokine production
- Reduced macrophage phagocytic capacity
- Delayed re-epithelialization
- Delayed collagen synthesis
- Delayed angiogenesis

Shaw et al, 2013

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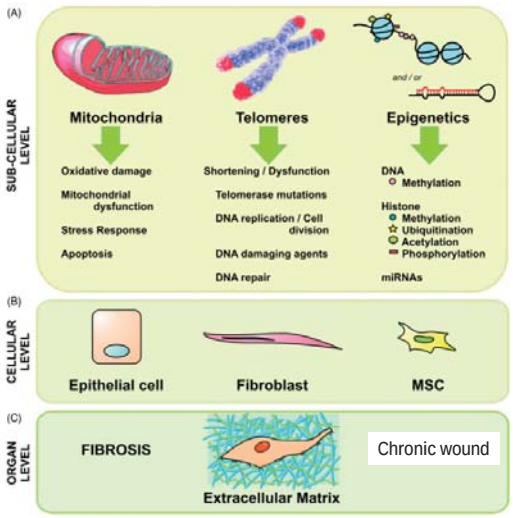
Multiple Biological Process are affected during aging



Kapetanaki et al, 2013

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Chronic Wounds: unmet medical need

Need for Improved Outcomes

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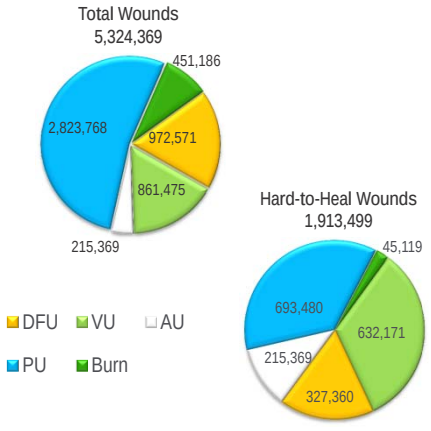
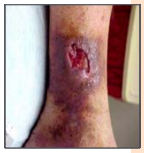
Cost of treating chronic wounds is rising sharply, representing >$25B in healthcare expenses in the US annually



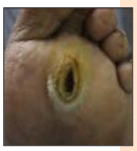
Venous leg ulcers



Standard of care
- Compression, dressings

Poor healing rates
- ~50% heal with standard of care
- Causes the loss of 2 million working days/ year in the US

Diabetic foot ulcers



Standard of care
- Offloading, dressings

Poor healing rates
- ~25 – 33% heal with standard of care
- >65,000 lower extremity amputations each year

Source: BioMedGPS SmartTRAK Wound Biologics database, 2012

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Challenges in Wound healing

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Some wounds fail to heal and become chronic. This may be due to various factors which can be patient-specific or wound-specific.

Characteristics of Chronic wounds:

- Cellular events: generally low mitotic activity, impaired migration, altered cellular phenotype..
- Wound environment : contaminated, biofilms, lack of blood supply, imbalance of matrix production and degradation …

Need for Tissue Regeneration

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Accelerating the Evolution of Wound Care

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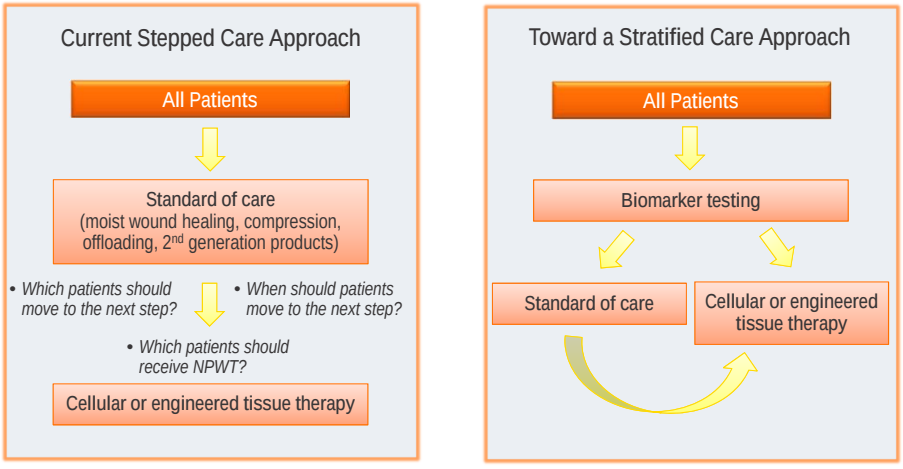

In clinical practice, use of cellular and engineered tissue therapies is combined with standard of care.
NPWT=negative pressure wound therapy

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TISSUE ENGINEERED PRODUCTS

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ACELLULAR SYNTHETIC

LYOFOAM EXTRA
SUPRATHEL

ACELLULAR BIOSYNTHETIC

BIOBRANE (B)
EZ-DERM (P)
INTEGRA (B)
JALOSKIN
LASERSKIN
HYALOMATRIX
TRANSCYTE (H)
XELMA

ACELLULAR BIOMATERIAL / TISSUE DERIVED

ALLODERM
ALLOPATCH
ALLOSKIN
ARTHROFLEX
DERMACELL
ENDOFORM (O)
FLEX HD (H)
GAMMAGRAFT
GRAFTJACKET
INTEXEN (P)
MATRIDERM (B)
MATRISTEM (P)
MATRIX HD
MEMODERM
OASIS (P)
PERMACOL (P)
PRIMATRIX (B)
PUROS DERMIS
REPLIFORM
STRATTICE (P)
TISSUEMEND (B)
UNITE BIOMATRIX (E)

CELLULAR BIOLOGICAL

Autologous , not cultured	
FULL THICKNESS GRAFT	FB KC
SPLIT THICKNESS GRAFT	FB KC
RECELL	KC
Autologous cultured	
BIOSEED-S	KC
CELLSPRAY	KC
EPIBASE	KC
EPISKIN	KC
HYALOGRAFT	FB KC
KERAGRAF (EPIDEX)	KC
LASERSKIN (VIVODERM)	FB KC
MYSKIN	KC
MYDERM	FB KC
PERMADERM	FB KC
Autologous cultured & Xenogeneic	
EPICEL	KC
Allogeneic minimally manipulated	
EPI-FIX	
GRAFFIX	
THERASKIN	
Allogeneic cultured	
CELADERM	KC
DERMAGEN	FB
ICX-SKN	FB
Allogeneic + synthetic	
DERMAGRAFT	FB
Allogeneic + xenogeneic	
APLIGRAF (B)	FB KC
ORCEL (B)	FB KC
Allogeneic immortal	
STRATAGRAFT	KC

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Example of Cellular Therapy: HP802

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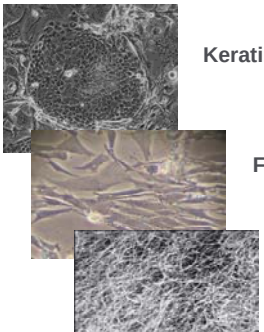
Allogeneic Cells and Matrix

- Component 1: Growth-arrested allogeneic keratinocytes and fibroblasts (1:9 ratio) in a solution of thrombin and cryo-protectant
- Component 2: Fibrinogen solution
- Component Vials stored at -80°C
- Cell Concentration: 0.5 million cells / mL (combined spray)

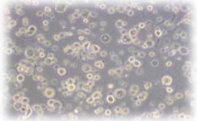
Spray Delivery

- Components sprayed sequentially onto ulcer
- Fibrinogen and thrombin form human fibrin provisional matrix



Keratinocytes

Fibroblasts



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HP802-247 Cell Dosing and Cell Ratio

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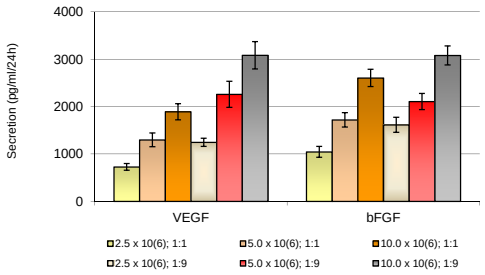
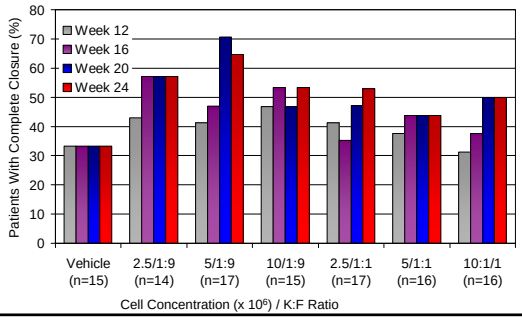


In vitro



In vivo

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Long term release of growth factors

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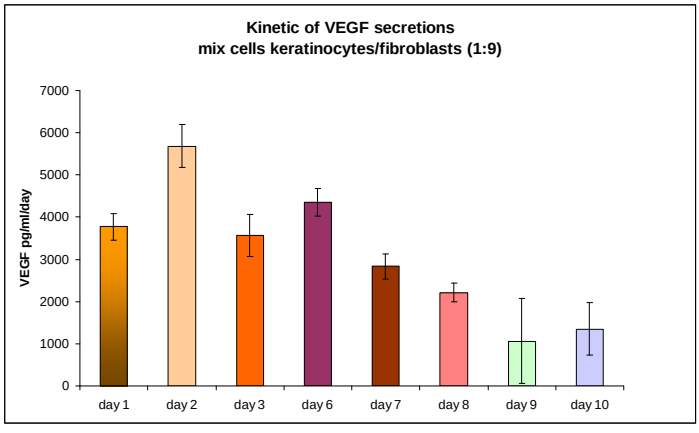

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HP802-247 Phase 2(b) Trial Results: The power of single cell suspension

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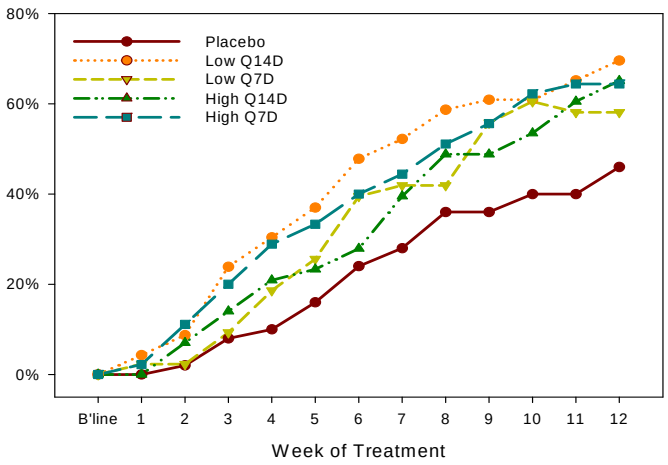
% of Subjects with Complete Wound Closure by Visit



Q14d=every 14 days, Q7d=every 7 days; significant differences from fibrin control (P<.05) observed for one or more dose groups at all follow-up weeks except 1-3.

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Cellular and Engineered Tissue Environment

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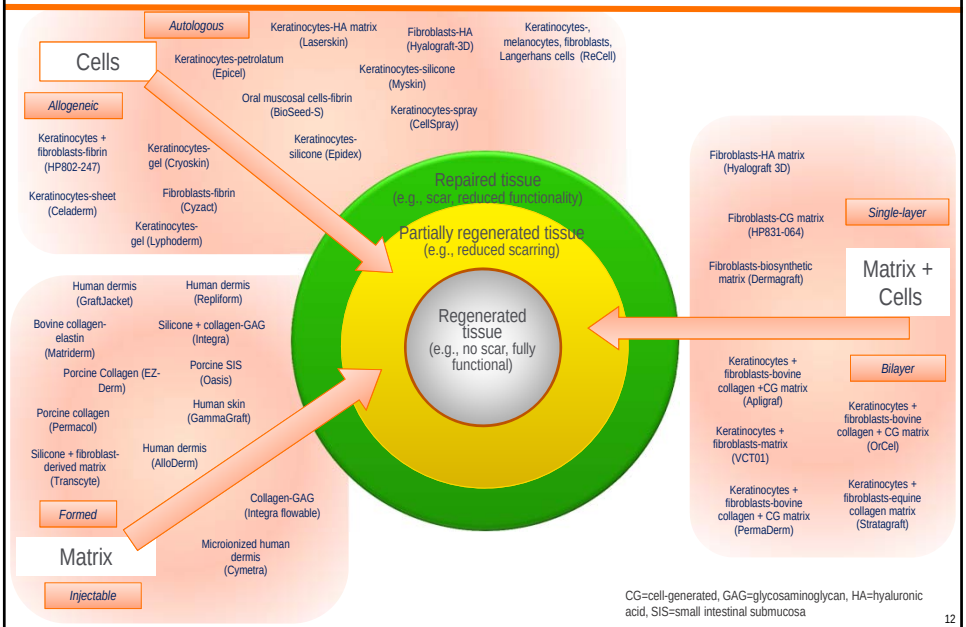

CG=cell-generated, GAG=glycosaminoglycan, HA=hyaluronic acid, SIS=small intestinal submucosa

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Future of Cellular Therapy

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Questions:
1- How to position cellular therapy?
2- What potency assays are relevant to regulate them?

Gaps:
1- Lack of clear mechanism of action
2- Time & Cost to develop a product from bench to bed side
3- Effect of Aging on efficacy

Opportunities:
1- The development of process and product development
2- Define specifically age-related mechanisms of healing

Priorities:
1- Provide clear definitions of the technologies to discriminate between cellular therapies, advanced therapies, dressing
2- Define a clear Regulatory and Reimbursement path
3- Development of evidence based therapy in the clinic

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