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MedicalDevice

Customer care

quality

factory

press release

red carpet

106 Products

91 Countries

One Brand

One Philosophy

PROMOITALIA
WELLNESS RESEARCH

Новый рубеж в эстетической медицине

Мезотерапия аутологичными клетками стромально-васкулярной фракции жировой ткани

PROMOBARREL - инновационный набор компании PROMOITALIA для аспирации жировой ткани и ее последующего очищения с целью извлечения мезенхимально-стромальной фракции адипоцитарного происхождения (ASCs)

Набор предназначен для:

Регенерации кожных покровов благодаря дифференцированным стромальным клеткам, секретирующим компоненты внеклеточного матрикса

Мезенхимально-стромальная фракция

Для того чтобы понять функционал и потенциал медицинского набора PROMOBARREL, изначально необходимо иметь представление о том что такое мезенхимально-стромальная фракция.

I

Молекулярная биохимия и физиология стромальных клеток

Стволовые клетки: типология и диффиренциация

Разновидности стволовых клеток:

1. *Эмбриональные стволовые клетки*
2. *Фетальные стволовые клетки*
3. *Постанатальные стволовые клетки*
4. *Взрослые стволовые клетки*

Стволовые клетки: типология и дифференциация

1. **Эмбриональные стволовые клетки** - недифференцированные клетки, которые также называются тотипотентными, и способные зарождать новые организмы и воссоздавать любые его клетки.

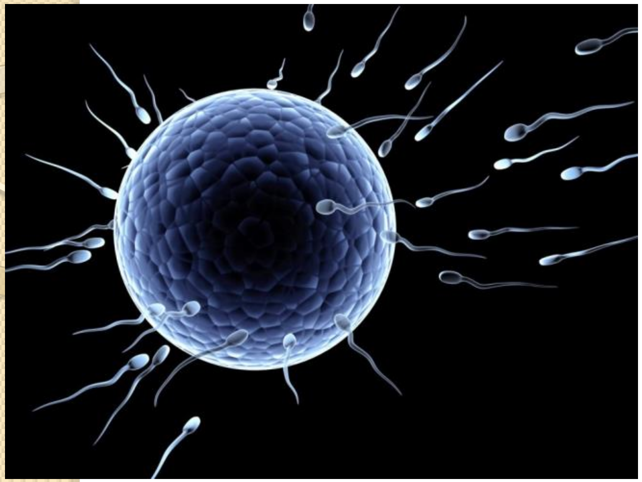
2. **Фетальные стволовые клетки** образуются на более поздних стадиях развития эмбриона и плода и обеспечивают рост ткани внутриутробно. Они обладают высоким дифференцировочным потенциалом после тотипотентных клеток.

Стволовые клетки: типология и дифференциация

1. **Постнатальные стволовые клетки** - клетки, которые дифференцируются в постнатальные образования, такие как пуповина, плацента, амниотический мешок. Эти клетки обладают различными характеристиками, могут быть полипотентными и монопотентными

2. **Взрослые стволовые клетки**, недифференцированные клетки определенного типа взрослого организма, которые могут спровоцировать рост одной или нескольких специфичных клеточных линий.

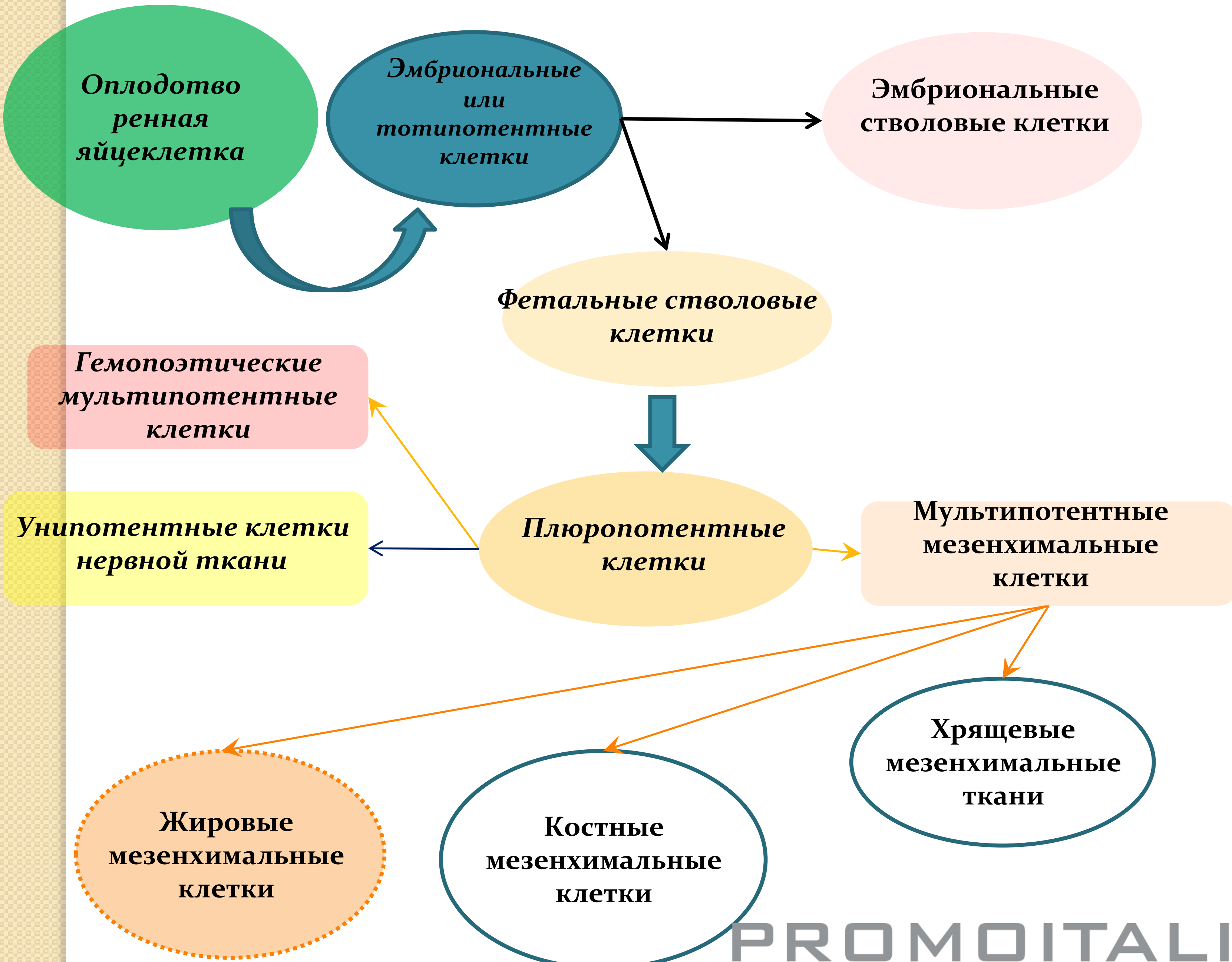
Оплодотворение



Тотипотентные стволовые клетки

Стволовые клетки, получаемые из источников постнатального происхождения

Взрослые стволовые клетки


Оплодотворенная яйцеклетка
Эмбриональные или тотипотентные клетки
Эмбриональные стволовые клетки
Фетальные стволовые клетки
Гемопоэтические мультипотентные клетки
Унипотентные клетки нервной ткани
Плюропотентные клетки
Мультипотентные мезенхимальные клетки
Хрящевые мезенхимальные ткани
Жировые мезенхимальные клетки
Костные мезенхимальные клетки

Различные типы клеток: сводные данные

• Стволовые клетки - недифференцированные клетки, которые могут развиваться либо по пути пролиферации и дифференциации

(Fuchs and Segre 2000; Mirzapour et al 2011).

• Мезенхимальные стволовые клетки (МСК) - не гемопоэтические стромальные клетки, обладающие способностью дифференцироваться в клетки различных тканей: костную, хрящевую и жировую.

(Zuck et al 2001).

• Мезенхимальные стволовые клетки (МСК) обладают способностью формировать в том числе фибробласты

(Kuznetsov et al. 1997).

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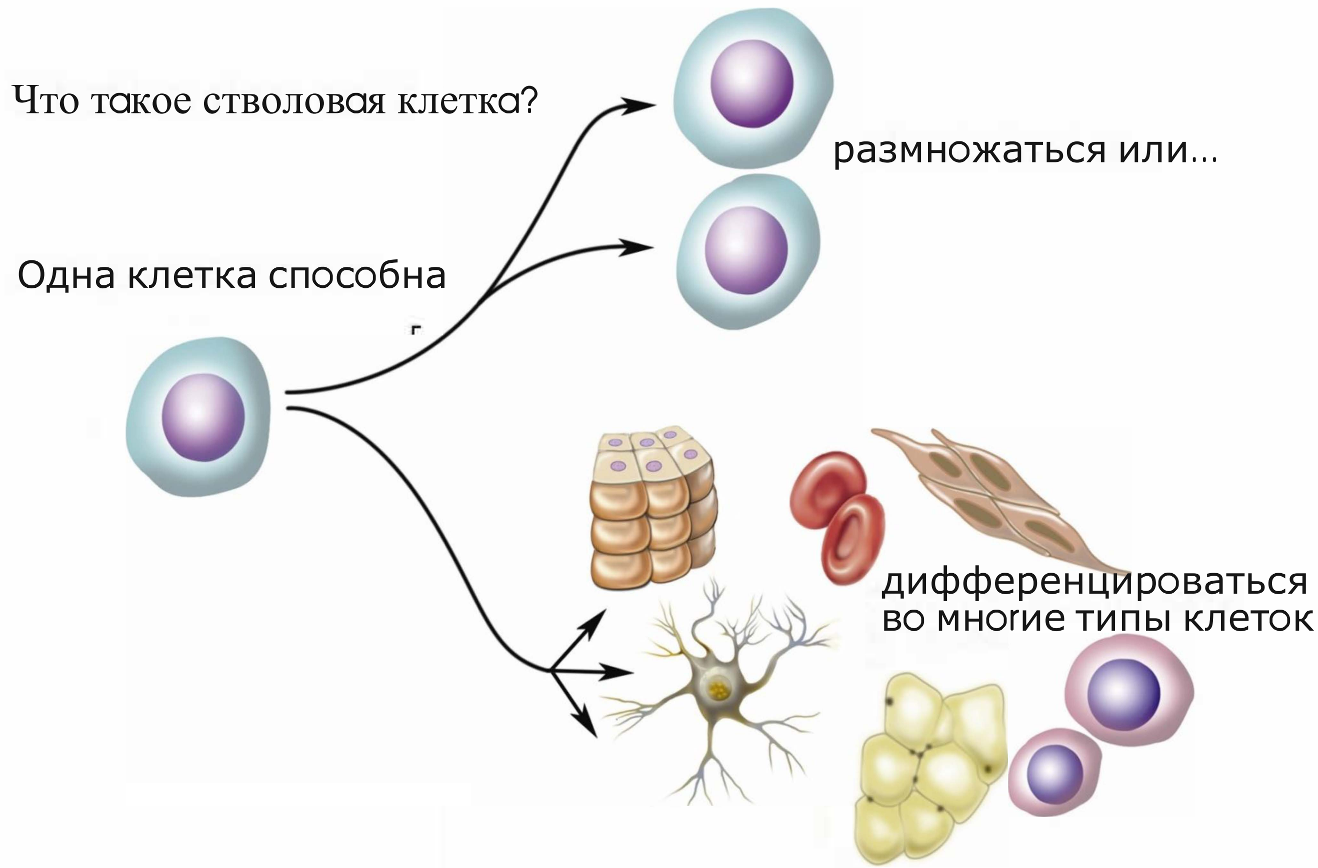
Особенности взрослых стволовых клеток

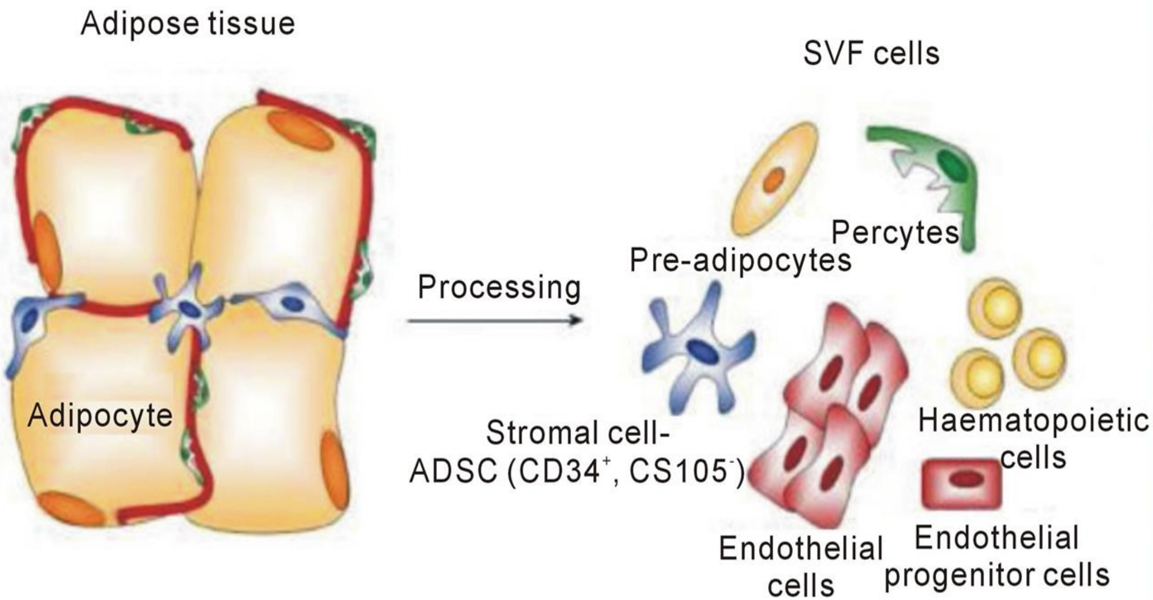
Стволовая клетка обладает способностью регенерироваться условно бесконечно.
При соответствующих условиях, следуя определенным стимулам, трансплантируемые клетки способны генерировать различные виды тканей.

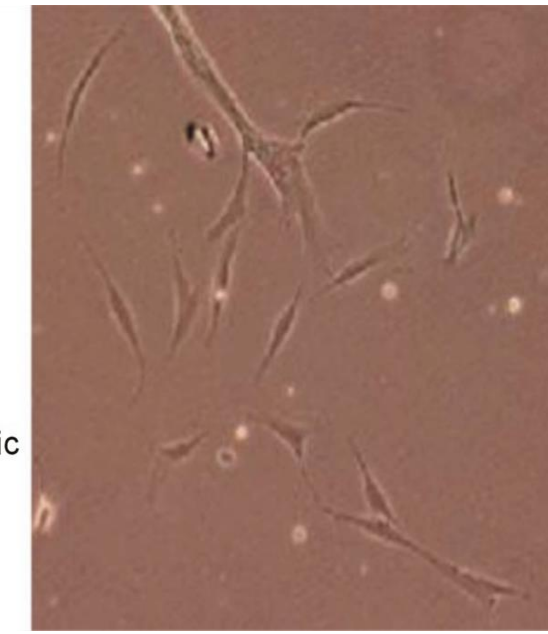
Особенности взрослых стволовых клеток:

- Бывают недифференцированные
- Обладают пролиферативной способностью
- Имеют возможность самообновляться
- Имеют способность генерировать дифференцированные клетки - предшественники


Что такое стволовая клетка?
Одна клетка способна
размножаться или...
дифференцироваться
во многие типы клеток

Компоненты жировой ткани





Stem cells of adipocyte origin: ASCs

Недавно наличие **мезенхимальных стволовых клеток** в значительных концентрациях было продемонстрировано в жировой ткани.

Полученные из жировой ткани клетки (ASCs) особенно эффективны поскольку способны дифференцироваться, не только во взрослые адипоциты, но и в фибробласты.

Наиболее важными стимуляторами способными трансформировать ASCs в адипоциты:

- инсулин
- глюкокортикостероиды.

Стволовые клетки жировой ткани: ASCs

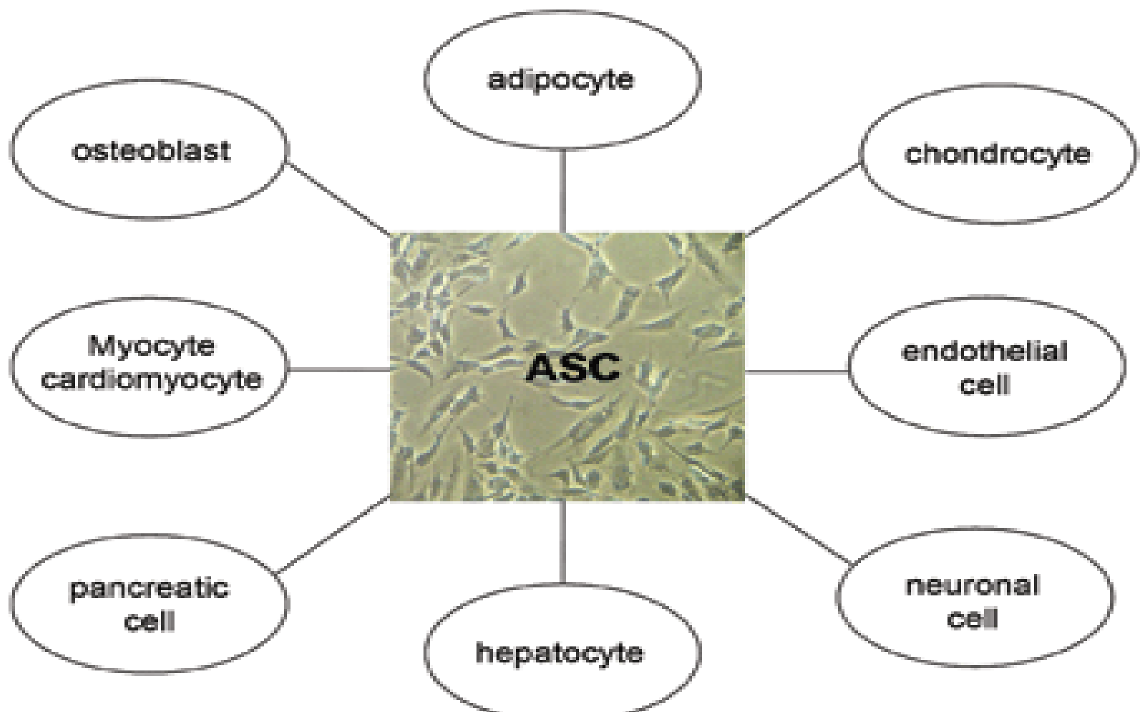
В жировой ткани содержится значительное количество **мезенхемальных стволовых клеток**, способных дифференцироваться как в зрелые адипоциты, так и в фибробласты.

Мезенхимально-стромальная фракция жировой ткани

ASCs

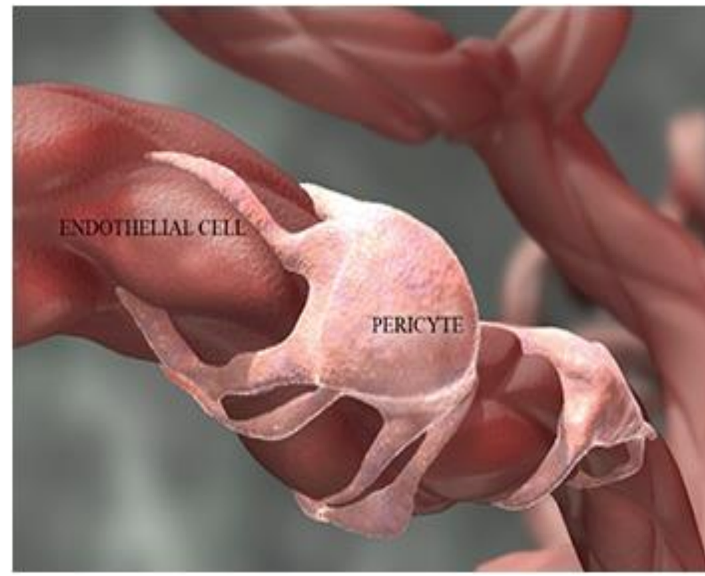
Наиболее важными стимуляторами способными трансформировать ASCs в адипоциты являются:

- **Инсулин**
- **Глюкокортикостероиды**



Значение клеток стромально-васкулярной фракции

Жировая ткань представлена не только жировыми и стволовыми клетками, но и клетками стромально-васкулярной фракции. Последние представляют собой следующие группы клеток:



- **Иные неопределенные стволовые клетки**

- **Клетки иммунной системы**

- **Эндотелиальные клетки/ Перициты** (отросчатые клетки, входят в состав стенок кровеносных сосудов)

- **Прогениторные клетки** (недифференцированные или ранние клетки-предшественницы)

- **Стромальные клетки** (соединительная ткань)

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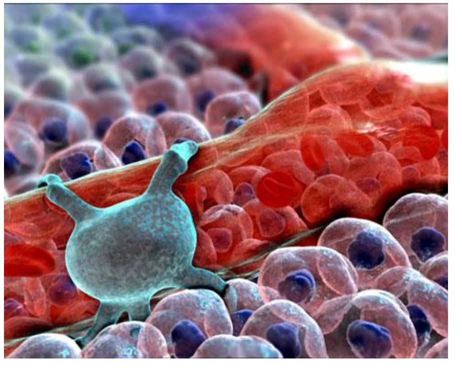
Значение стромально-васкулярной фракции

Почему клетки стромально-васкулярной фракция играет значительную роль в процессе регенерации тканей?

В следствие повреждения сосуда перициты отделяются из эндотелия и являются частью мезенхимально –стромальной фракции.

Эти клетки вырабатывают вещества, которые активно участвуют в регенерации клеток, стимулируя неоангиногенез.



Факторы роста способствуют восстановлению дермальной ткани и новых кровеносных сосудов, что приводит к регенерации ткани в области имплантации.

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Значение стромально-васкулярной фракции

Почему стромально-васкулярная фракция играет значительную роль в процессе регенерации тканей?

Стволовые клетки и перициты, в зависимости от ткани, в которой они находятся, генерируют высокие концентрации факторов роста, такие как:

EGF - Эпидермальный фактор роста

- VEGF - Васкулярный эндотелиальный фактор роста
- bFGF - Фактор роста фибробластов
- KGF - Фактор роста кератиноцитов
- PDGF - Тромбоцитарный фактор роста
- HGF - Фактор роста гепатоцитов
- TGF-b - Трансформирующий фактор роста
- IGF - Инсулиновый фактор роста
- BDNF - Нейротрофический фактор роста

Вышеперечисленные факторы роста помогают восстановить покровную ткань и образуют новые кровеносные сосуды с последующей регенерацией тканей в области имплантации

Использование клеток мезенхимально-стромальной фракции в регенеративной терапии

В последние годы к ASC спровоцирован большой интерес в научном ландшафте, поскольку они способны трансформироваться в клетки различного типа, тем самым оказывая позитивное воздействие на различные заболевания.

Стоит отметить, что лечебный эффект проявляется только в том случае, если концентрация этих клеток высока.

Использование клеток мезенхимально-стромальной фракции в регенеративной терапии

Именно с помощью уникального набора компании PROMOITALIA - PROMOBARREL - возможно получить достаточное количество мезенхимальностромальной фракции, используемой в целях регенеративной терапии.

"Изученное количество гомогенных мезенхимально-стромальных клеток необходимых для использования в медицинских целях приведено в следующей статье" (Rosland et al 2009)

Количественное содержание ASCs в жировой ткани

Среднестатистичекое количество ASCs в жировой ткани у здорового человека в возрасте от 45 до 50 равно 200 x 10^6

Cytotherapy. 2004;6(1):7-14.

Yield of human adipose-derived adult stem cells from liposuction aspirates.

Aust L[1], Devlin B, Foster SJ, Halvorsen YD, Hicok K, du Laney T, Sen A, Willingmyre GD, Gimble JM.

⊕ Author information

Abstract

BACKGROUND: Primary cultures of isolated human adipose-derived adult stem (ADAS) cells are multipotent and differentiate in vitro along the adipocyte, chondrocyte, neuronal, osteoblast, and skeletal muscle pathways.

METHODS: We examined the ADAS cell yield per unit volume of liposuction tissue, and their surface protein phenotype by flow cytometry. Adipogenesis was assessed by Oil Red O staining and ELISA analysis of leptin secretion.

RESULTS: The donor population was 87.5% female (n=18) with a mean age (+/-SD) of 44+/-10 years and body mass index (BMI) of 24.9+/-2.7. The mean cell yield was 404 000+/-206 000 cells per milliliter of lipoaspirate (n=18). Linear regression analysis of the cells derived from the female donors demonstrated a significant negative correlation between the number of cells obtained per milliliter of lipoaspirate with the BMI but not the age of the donor. The undifferentiated ADAS cells were homogeneously positive for the cell-surface markers CD10, CD13, CD29, CD44, CD49e, CD59, CD90, and HLA-ABC, and homogeneously negative for the cell surface markers CD11b, CD45, and HLA-DR. The absence of the panhematopoietic marker, CD45, indicates that the ADAS cells do not derive from circulating BM hematopoietic stem cells. Adipocyte differentiation led to a 5.1-fold increase in Oil Red O staining, and a 196-fold increase in leptin secretion levels. Culture of the cells in the presence of antibiotic and fungizone did not alter the undifferentiated ADAS cell immunophenotype based on flow cytometry, or their adipocyte differentiation based on leptin secretion.

PROMOBARREl: качественные анализы, научные исследования

В 2013 году PROMOITALIA провела качественный анализ с целью проверки наличия клеток мезенхимально-стромальной фракции жировой ткани, извлеченных и отделенных с помощью набора PROMOBARREL.

DEPARTMENT OF SCIENCE AND ENVIRONMENTAL BIOLOGICAL AND PHARMACEUTICAL TECHNOLOGY

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Naples, May 29th 2013

SCIENTIFIC REPORT ON ADIPOSE STEM CELLS AND LIPOFILLING BY PROF. ALFONSO BALDI ON BEHALF OF PROMOITALIA GROUP SPA, USING THE KIT
M”

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PROMOBARREL: качественные анализы, научное исследование

Seconda Università degli Studi di Napoli
SUN

DEPARTMENT OF SCIENCE AND ENVIRONMENTAL
BIOLOGICAL AND PHARMACEUTICAL TECHNOLOGY

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Conclusions

The results obtained allow to confirm that the method described is able to isolate from the adipose tissue positive cells for the expression of beta integrin 1, which is a well-described marker of adipose stem cells.

PROMOBARREL: качественные анализы, научное исследование

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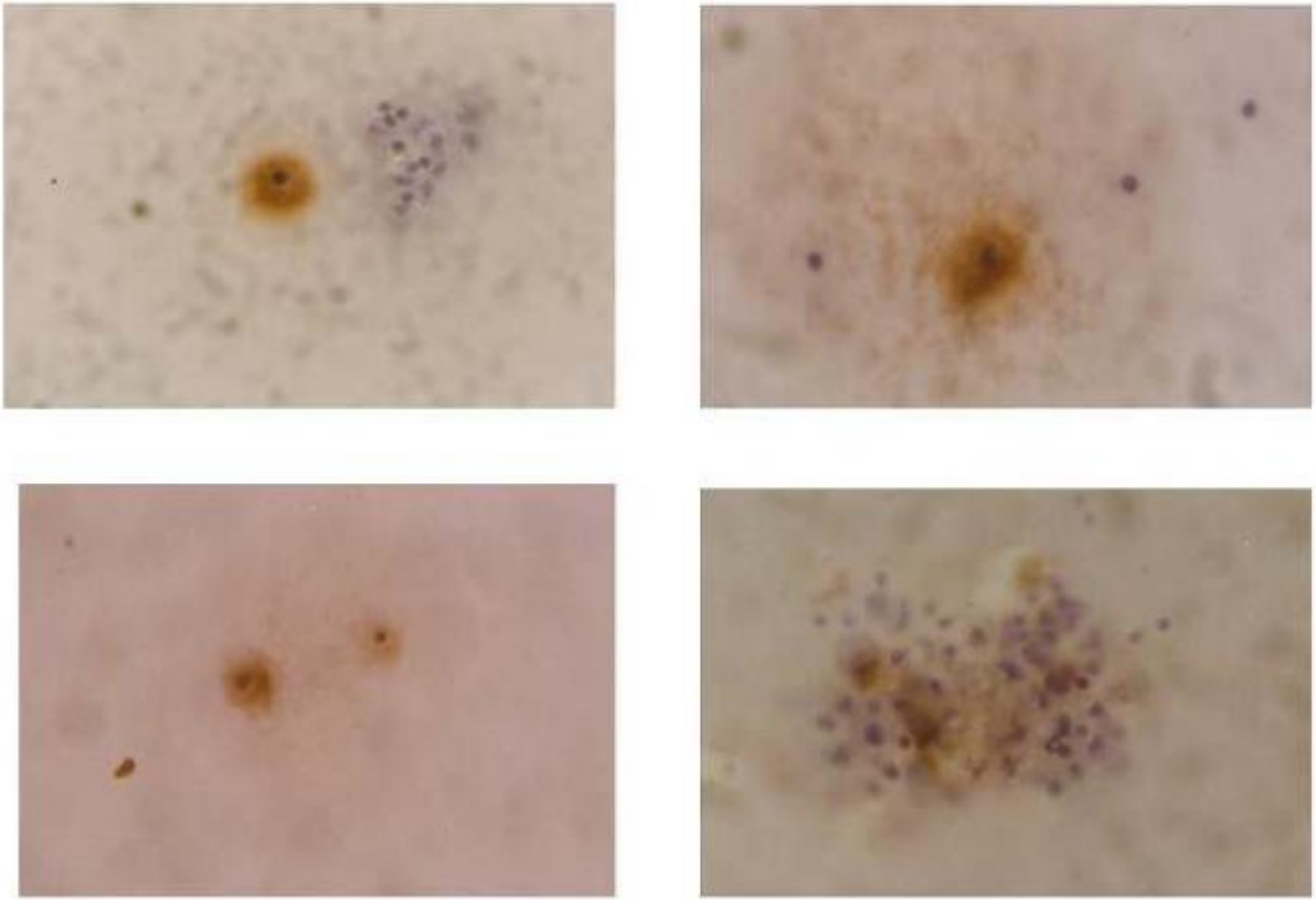
Стволовые клетки жировой ткани были идентифицированы благодаря бета-интегринам, селективным молекулам, способным связываться только с ASCs.

Наличие радиолюминесцентных маркеров выявлено и подтверждено в данной научной статье

Клетки ASCs с аккумулированы в глубоком слое и их забор достаточно прост.

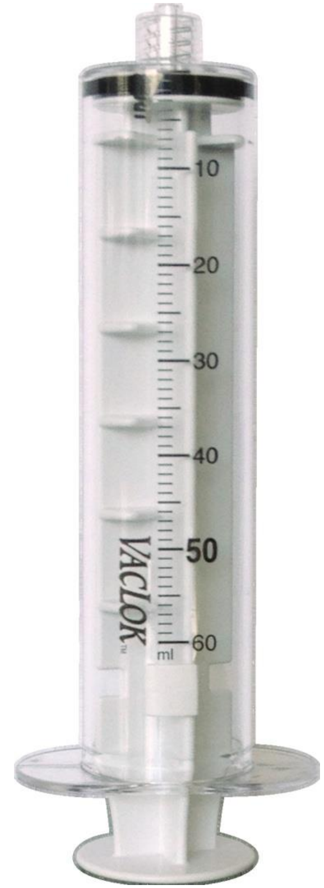
Иммуноцитохимическая оценка экспрессии интегрина-бета в стромально-васкулярной фракции жировой ткани

Коричневый окрас демонстрирует позитивную реакцию, подтверждающему наличие МСК.



Медицинское изделие “KIT”

PROMOBAREL



Каждый набор состоит из:

- **1 шприц VACLOK для аспирации жировой ткани**
- **1 PROMOBARREL - Контейнер**
- **1 Винтовой поршень**
- **2 Коннектера LUER LOCK**

Описание процедуры

1. Идентификация места аспирации
2. Приготовление местной анастезии (смесь раствора 20 мг/мл мепивакаина гидрохлорида с адреналином 1: 100000)
3. Аспирация 20 - 40 мл жировой ткани с помощью Vaclock шприца
4. Транспортирование забранной ткани при помощи Луер Лок коннектора в контейнер - Promobarrel

Описание процедуры

5 Центрифугирование (2500/3000 об/мин в течение 7-8 минут) для разделения аспирированной ткани на слои.

6 После центрифугирования с помощью винтового поршня трансплантируем содержимое пробирки в шприц соединенный при помощи Luer Lock коннектера, за исключением слоя богатого стромально-васкулярными клетками.

7 Клетки забираем в шприц и вводим внутрикожно.

Описание процедуры

Идентификация места аспирации

2. Приготовление местной анастезии (смесь раствора 20 мг/мл мепивакаина гидрохлорида с адреналином 1: 100000)

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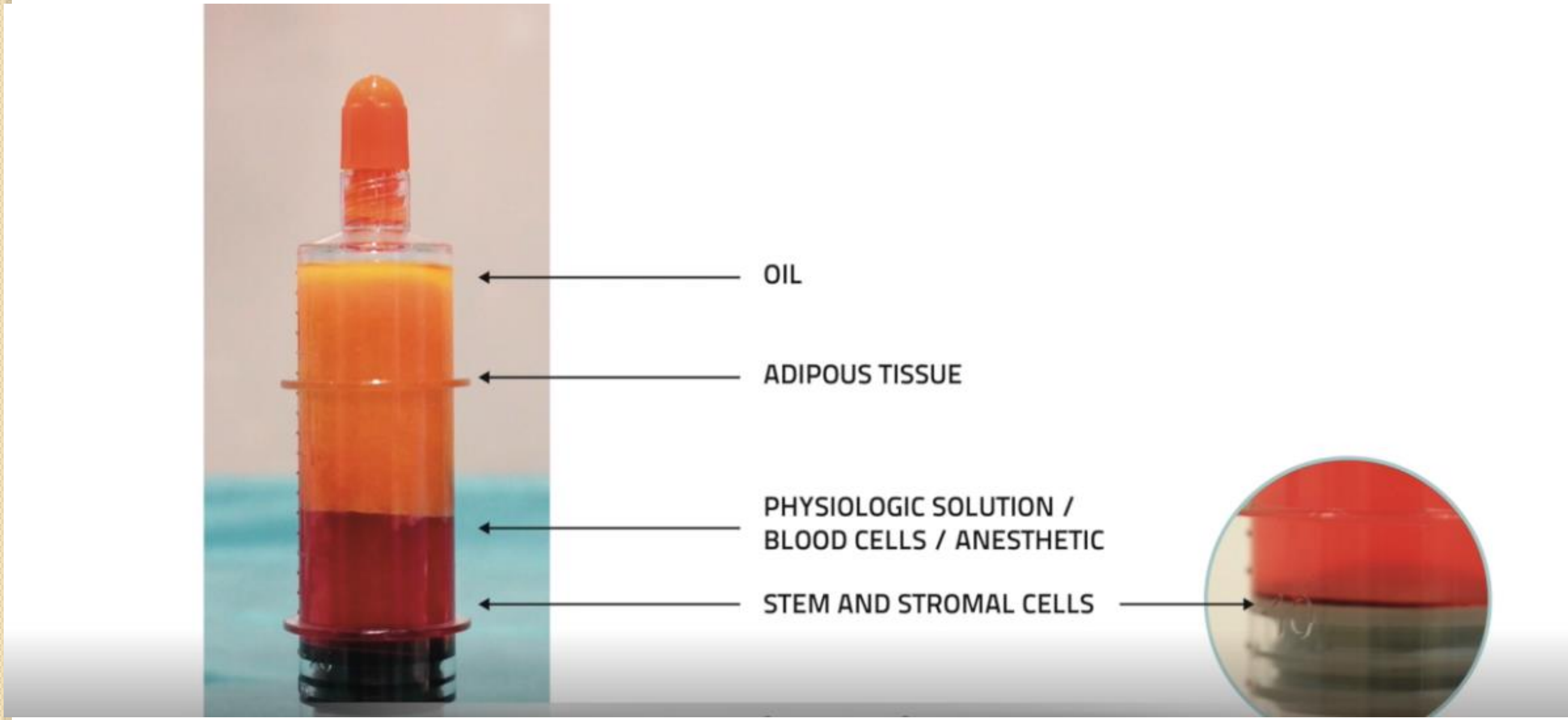
Описание процедуры

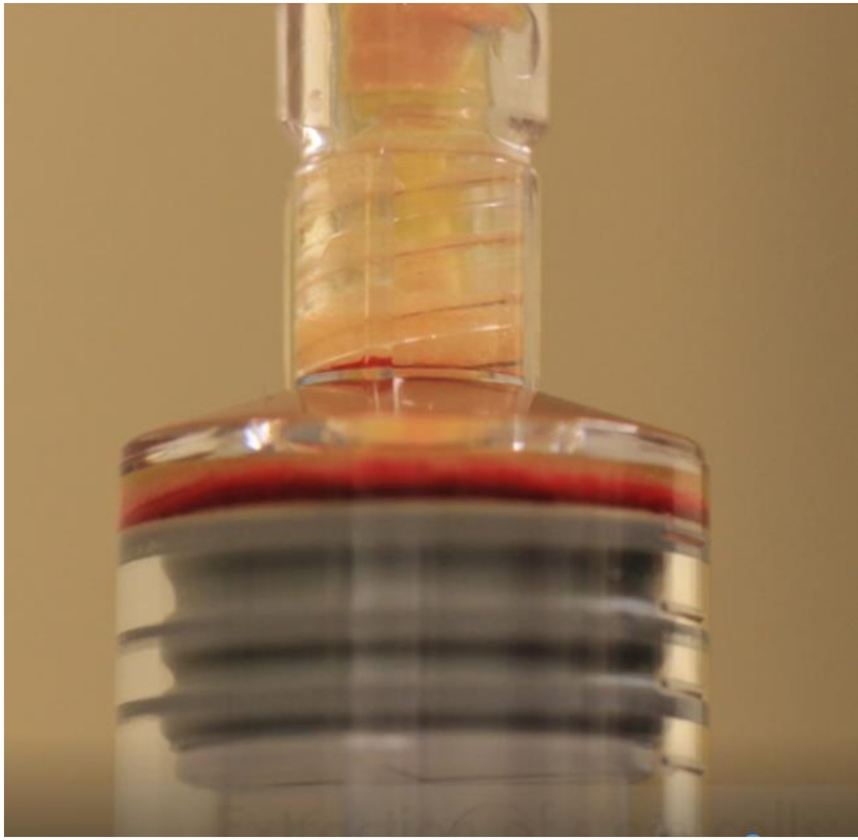
3. Аспирация 20 - 40 мл жировой ткани с помощью Vaclock шприца

4.Транспортирование забранной ткани при помощи Луер Лок коннектора в контейнер - Promobarrel

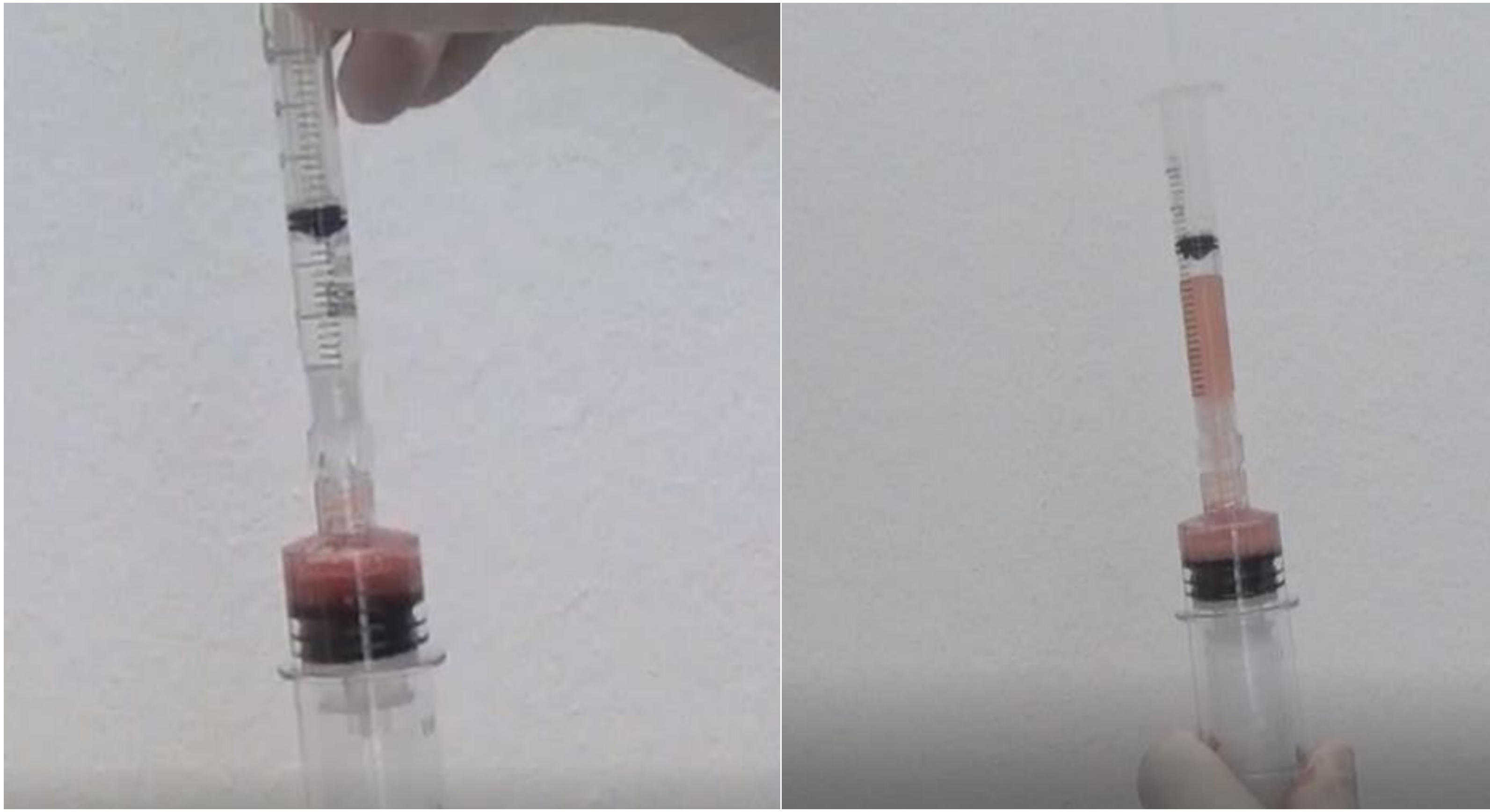
Центрифугирование (2500/3000 об/мин в течение 7/8 мин) для разделения аспирированной ткани на слои



Сепарированный раствор послойно



После центрифугирования с помощью винтового поршня трансплантируем содержимое пробирки в шприц, соединненый при помощи Luer Lock коннектера, за исключение слоя богатого стромальными клетками.



Разведение стромально-васкулярной фракции с физиологичным раствором

Забираем полученный раствор в шприц и вводим внутрикожно.

Показания и назначение

Регенеративный раствор на основе клеток стромально-васкулярной фракции показан к применению в следующих целях:

- Регенерации тканей лица
- Регенерации кожи шеи и декольте
- Регенерации кожи рук и стоп
- Лечения стрий
- Лечения аллопеции

Протоколы, рекомендации и предложения

Клетки стромально-васкулярной фракции значительно повышают свою активность, если количество свободных радикалов в тканях низкое.

По этой причине, возможно предложить пациенту диету богатую антиоксидантами, минимум за 15 дней до момента проведения процедуры.

Протоколы, рекомендации и предложения

При необходимости (пациентам, подвергшимся значительному оксидантному стрессу) предложить к диете пищевую добавку коэнзим Q10. Для того, чтобы ускорить процесс, возможны комбинированные методы, такие как озонотерапия одновременно с диетой.

Терапию возможно проводить 2 раза в год с интервалом в 6 месяцев.

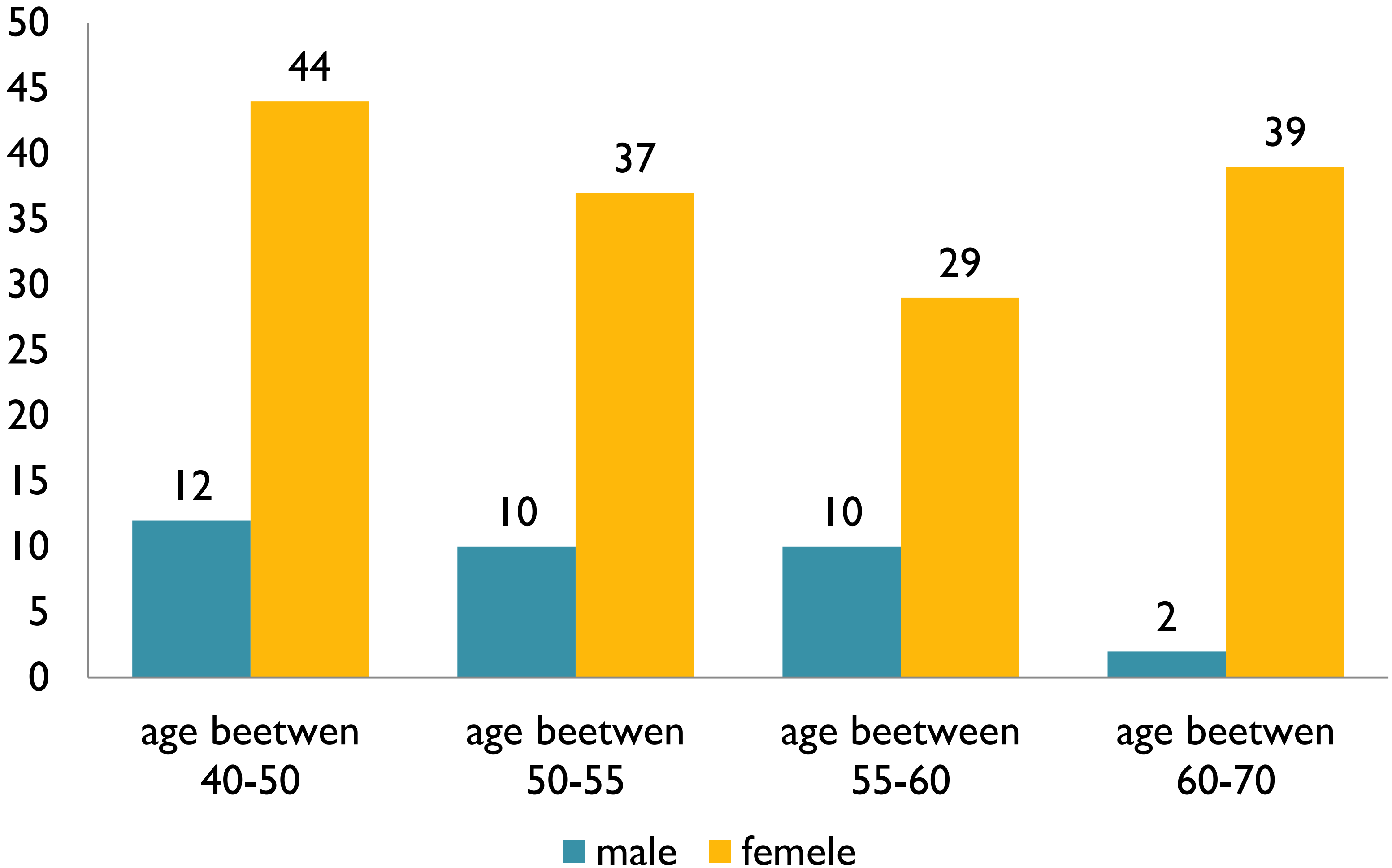
Клинические случаи

За последние два года в клинический эксперимент были вовлечены:

- 183 пациента
- Пациенты обоих полов
- Пациенты в возрасте от 42 до 70

Процедура была проведена в области лица и декольте с целью устранения эстетических недостатков.

Пол-Возраст



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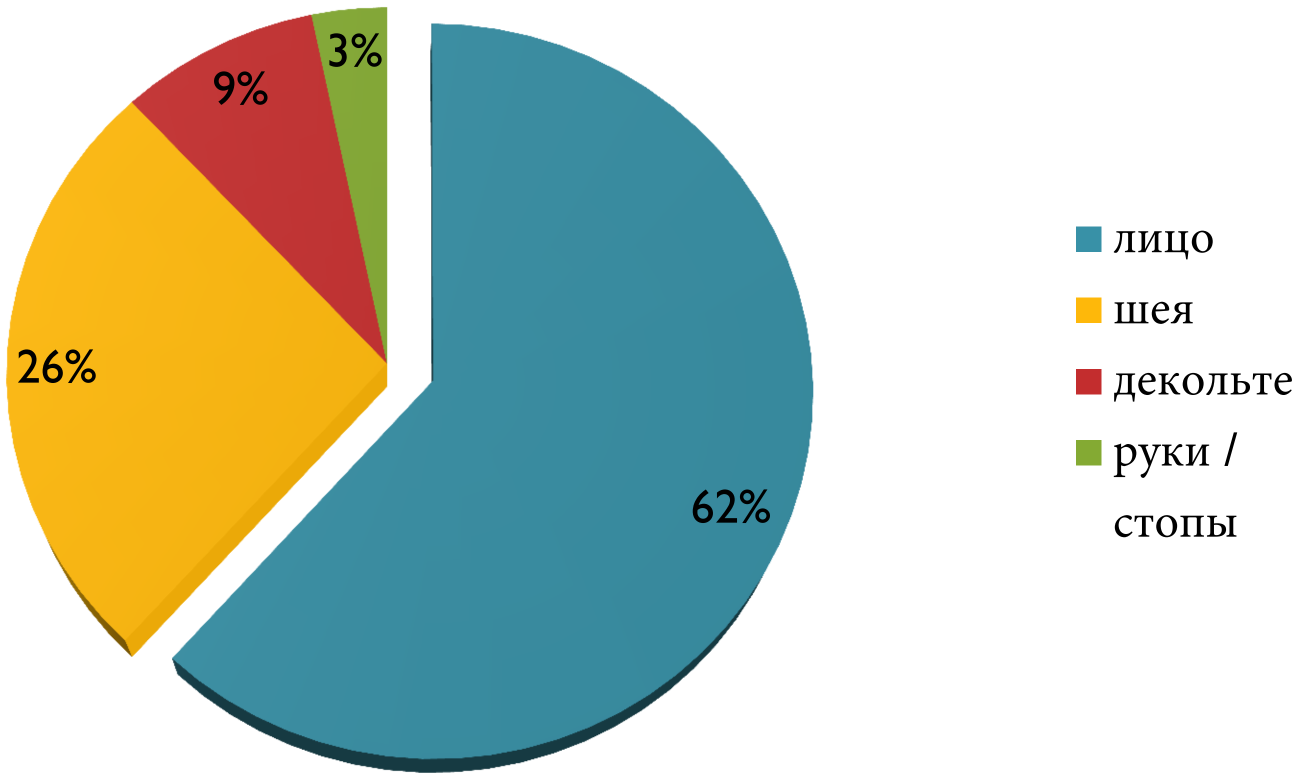
Пол-Возраст



Клиническое исследование оценивалось по следующим критериям:

- ✓Визуальная оценка эффективности врачом-дерматологом
- ✓Гистологическое исследование
- ✓Переносимость мезотерапевтического коктейля под контролем дерматолога
- ✓Измерение с помощью специальных инструментов (УЗИ аппарата, методом Пликометрии)
- ✓Заключение врача
- ✓Анализ статистических данных на проверку эффективности

Клинический инструментарий:

- УЗИ: измерение толщины кожи
- Пликометрия: измерение толщины и плотности кожи
- Морфометрия : измерение окружности обрабатываемых участков
- Эластометрия: измерение вязкоэластичных характеристик инъецированной зоны

Материалы и методы

Для оценки эластичности кожи использовался прибор MPA580 Microcaya ™ .

Для оценки плотности кожи был использован прибор GIMA 27320 ™

Для ультразвукового исследования использовали прибор ESAOTE MyLab™Alpha

Результаты

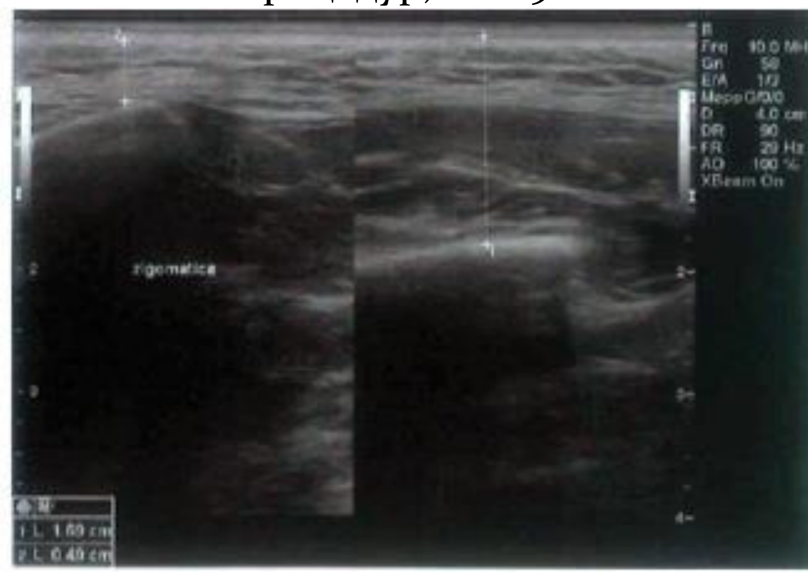
Возраст	Ультразвуковой тест после процедуры: средний % улучшения показаний	РПликометрическое измерение после процедуры: средний % улучшения показаний	Морфометрическое измерение: средний % улучшения показаний	Измерение вязкоэластичных свойств средний % улучшения показаний	Итоговое субъективное заключение
Age 40-50	65%	76%	23%	74%	91%
Age 50-55	59%	61%	10%	61%	93%
Age 55-60	43%	48%	11%	42%	88%
Age 60-70	38%	22%	8%	11%	87%

Результаты

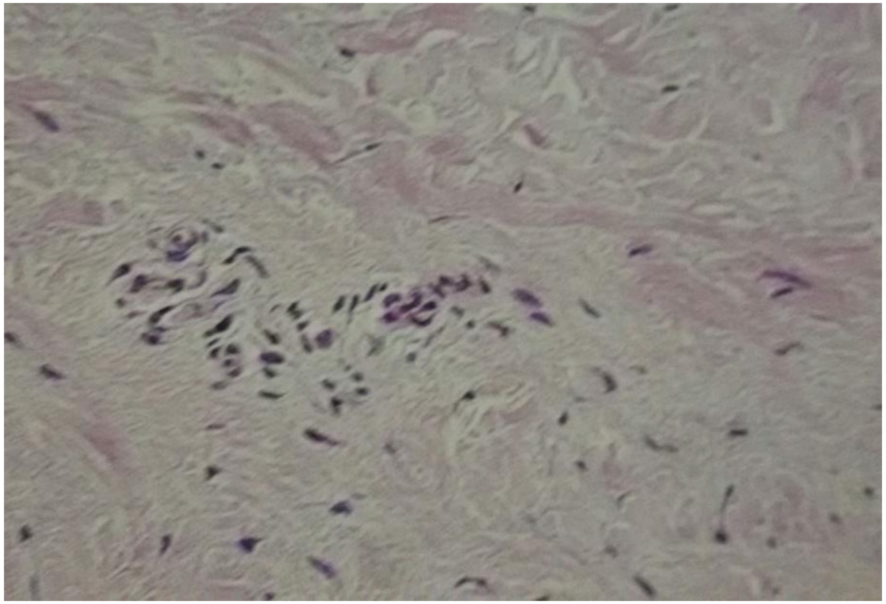
Скуловая область: ультразвуковое обследование

До лечения– 0.94 mm.:

После полного курса терапии (курс из 6 процедур) – 1.69 mm.

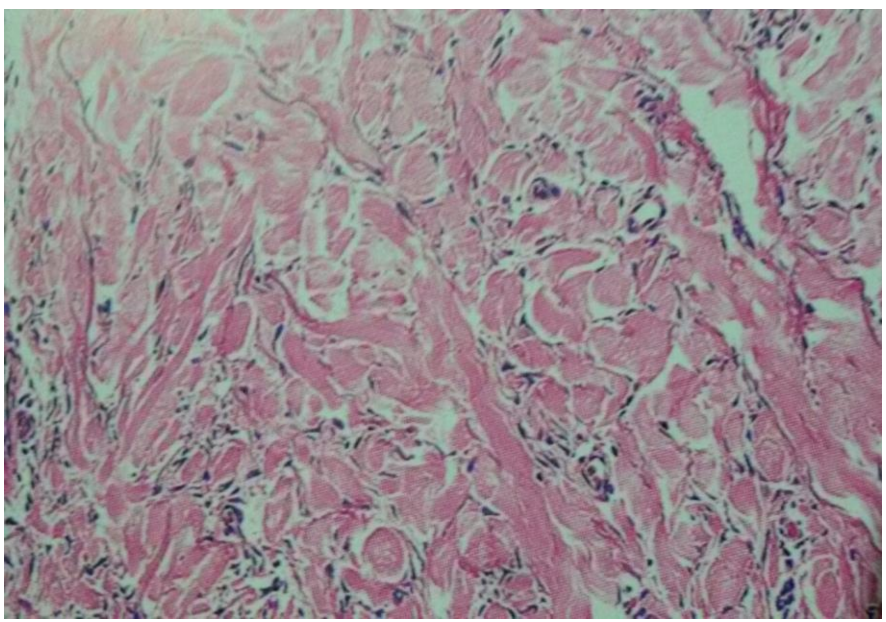


Анализ полученных данных демонстрирует, что после терапии увеличивается толщина дермы за счет стимуляции фибробластов и возрастает межклеточный матрикс.



Гистологическое заключение

Пациент в возрасте 43 лет до инъецирования коктейля на основе ASCs в скуловой области



Спустя 3 месяца после имплантации

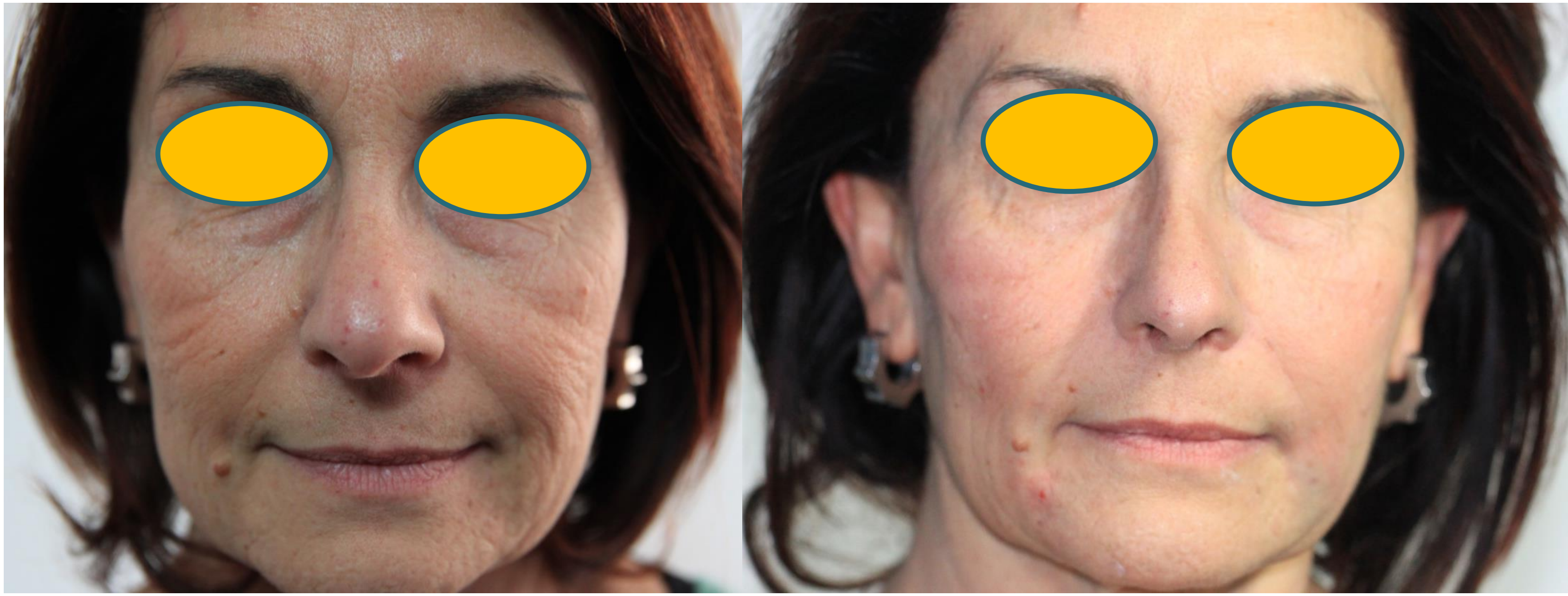
Заключение

Анализ полученных данных показывает, что использование мезотерапевтического коктейля значительно улучшает качество и эластичность кожи. Результаты оценки относятся к группе пациентов в возрасте от 40 до 50 лет. Однако, субъективная оценка позволяет сделать вывод, что процедура приемлема для всех возрастных групп.

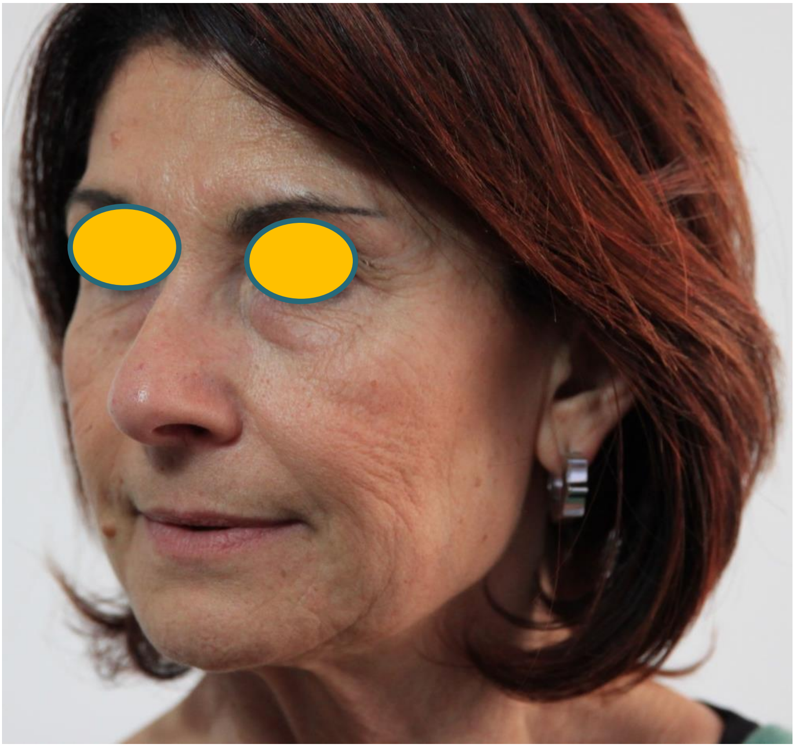
Практика терапевтического использования доказывает высокую удовлетворенность пациентов, максимальную эффективность, безопасность и отсутствие сложности использования.

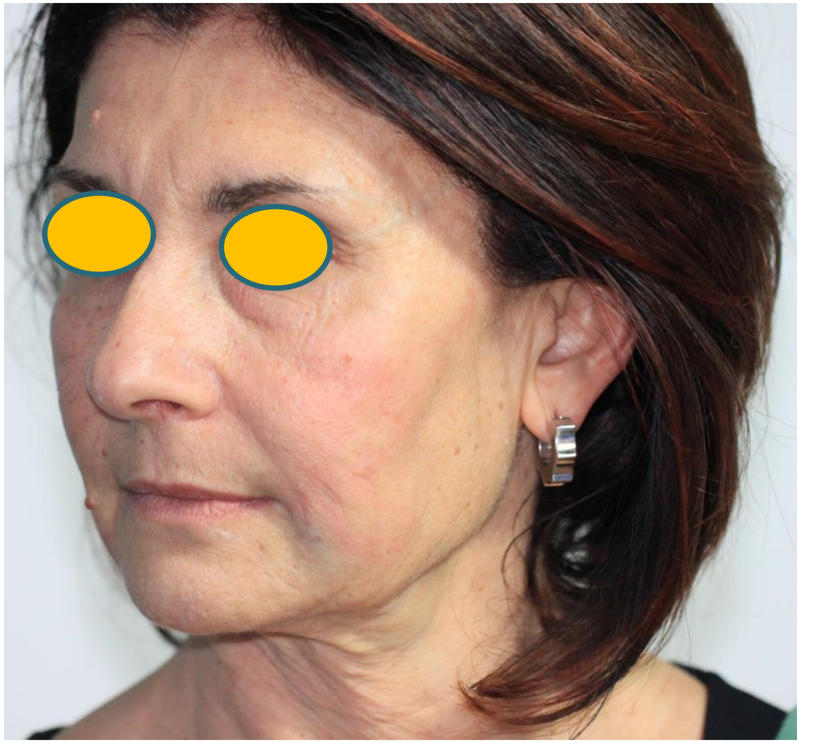
Фотографии до/после

до и спустя 3 месяца после проведения процедуры



До и спустя 3 месяца после проведения процедуры





До и спустя 6 месяцев после проведения процедуры

До и после проведения двух процедур с интервалом в 6 месяцев

До и после проведения двух процедур с интервалом в 6 месяцев

Библиография

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Antiwrinkle effect of adipose-derived stem cell: Activation of dermal fibroblast by secretory factors

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ABSTRACT

Background: Adipose-derived stem cells (ADSC) have wound-healing and antioxidant effects on human skin via secretion of growth factors and activation of dermal fibroblasts.
Objective: Paracrine mechanism reducing ultraviolet-B (UVB)-induced wrinkles by ADSC is investigated in this study.
Methods and Results: Wrinkles were induced by an eight-week UVB irradiation, and were significantly improved by the subcutaneous injection of ADSC in hairless mice. In a replica analysis, parameters involving wrinkles were improved with mid-level and high doses of ADSC (1×10^4 and 1×10^5 cells). Dermal thickness and collagen contents in the dermis also were increased in the ADSC-injected groups. To characterize the paracrine mechanism involving the antiwrinkle effect of ADSC, a conditioned medium of ADSC (ADSC-CM) was directly incubated in human dermal fibroblasts (HDF). UVB irradiation reduced the proliferation of HDF, but this was reversed by the pretreatment of ADSC-CM in a dose-dependent manner. In a cell cycle analysis, ADSC-CM decreased the UVB-induced apoptotic cell death, which was demonstrated by the reduced sub-G1 phase of HDF. In addition, the ADSC-CM increased the protein expression of collagen type I and decreased the protein level of matrix mataloproteinase 1 in HDF, which may account for the increased collagen contents in the dermis.
Conclusions: Collectively, these results indicate that the ADSC and its secretory factors are effective for UVB-induced wrinkles, and the antiwrinkle effect is mainly mediated by reducing UVB-induced apoptosis and stimulating collagen synthesis of HDF.

Adipocyte-Derived Stem and Regenerative Cells in Facial Rejuvenation

Steven R. Cohen, MD[a,b,c,*], Brian Mailey, MD[a]

KEYWORDS

• Adipocyte • Stem cells • Regenerative • Facial aging • Fat graft • Revolumization

KEY POINTS

- Current methods of producing cell-enriched fat include isolating adipose-derived regenerative cells (ADRC) using a commercial collagenase enzymatic digestive system and then recombining the isolated cells with traditional lipoaspirated fat.
- Cell-enriched fat should be delivered in small concentrated aliquots of fat per unit area of native tissue to optimize engraftment. Initial reports using these methods demonstrate promising results for multiple applications.
- A key to optimizing engraftment includes concentrating the fat per unit volume of graft delivered per area of native tissue in the correct proportions to maximize the surface area of grafted fat and prevent large clumpy deposits.
- The exact fate and regenerative effects of autotransplanted ADRC are still unknown and much work still needs to be done.

Minimally Invasive Rejuvenation of the Face and Neck

Editor

KENNETH O. ROTHAUS

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The Potential of Adipose Derived Regenerative Cells for Non-Healing Wounds

Background

The complex nature of wound healing carries with it implicit vulnerabilities such that, under certain circumstances, progression through the different phases of healing can be protracted or even arrested resulting in development of a chronic wound. By definition, a chronic wound is a wound that does not heal within the initial 3 month period[1] and affects greater than 6.5 million patients in the USA alone[2]. Complicating circumstances that cause a delay or obstruction of the natural wound healing response include peripheral vascular disease, spinal cord injury, complications associated with burns, diabetes, obesity and prior exposure to irradiation. In such settings, there is evidence that cells within the wound that are responsible for healing exhibit functional impairment. Consequently, delivery of supplemental cells with the capacity to promote healing has the potential to treat chronic wounds.

Adipose Tissue as a Regenerative Cell Source

The concept that adipose tissue contains cells with broad potential for regenerative medicine had its beginnings in a paper in the journal Tissue Engineering published in 2001[3]. In this work the authors placed cells obtained from human adipose tissue in culture and showed that the cultured cell population possesses a key characteristic of stem cells; it can differentiate into cells of multiple lineages. This study is the most cited paper in the history of Tissue Engineering having been cited over 900 times; it is still among the journal's most frequently downloaded papers. The following year the same research team published a follow-up study that proved that the property of multilineage differentiation was possessed by single cells within the cell population thus proving that there are stem cells in human adipose tissue[4]. The cultured cell population is usually described in the literature as Adipose-Derived Stem Cells (ADSCs). ADSCs have many properties in common with a related cell type cultured out of bone marrow that is generally referred to as Mesenchymal Stem Cells or Marrow Stromal Cells (MSCs). For example, both cell types can differentiate along osteogenic, adipogenic, chondrogenic, and myogenic lineages[4-6] and express similar, though not identical, cell surface markers[7].

As research into adipose stem cells continued it became apparent that the cell population used to start the cultures had properties that could be valuable in the clinic. First, it contains stem cells that can be grown up in culture to generate ADSCs. In fact, adipose tissue is the richest known source of adult stem cells which usually comprise around 1-2% (and as much as 5%) of the starting population obtained from adipose tissue[8,9]. This compares very favorably with age-matched marrow in which MSCs usually comprise only 0.0004% of cells[10]. Second, the cell population used to start ADSC cultures also contains other cells that have potentially useful properties including endothelial progenitor cells, tissue resident macrophages, pericytes endothelial cells, and smooth muscle cells. For this reason we refer to this non-cultured cell population as Adipose-Derived Stem and Regenerative Cells (ADRCs). A table of the average composition of the cell population is shown in **Table 1**.

Table 1: Composition of Adipose-derived regenerative cells

Cell Type	Average Frequency
Endothelial cells	7%
Smooth muscle cells	9%
Blood cells	22%
Tissue Macrophages	23%
Other (CD34+/CD31-/CD45-)	38%

Aesthetic Surgery Journal

http://aes.sagepub.com/

Autologous Fat Transplantation Versus Adipose-Derived Stem Cell–Enriched Lipografts : A Study

Aris Sterodimas, Jose de Faria, Beatriz Nicaretta and Filippo Boriani

Aesthetic Surgery Journal 2011 31: 682
DOI: 10.1177/1090820X11415976

Proliposterm: scientific study

Adipose-Derived Stem and Progenitor Cells as Fillers in Plastic and Reconstructive Surgery

Timothy A. Moseley, Ph.D.
Min Zhu, M.D.
Marc H. Hedrick, M.D.

San Diego and Los Angeles, Calif.

Summary: Plastic surgeons are keenly aware of the principle "replace like with like." This principle underlies much of the rationale behind the clinical use of autologous fat transplantation, despite the procedure's drawbacks. Autologous fat transplantation is frequently used for a variety of cosmetic and reconstructive indications not limited to posttraumatic defects of the face and body, involutional disorders such as hemifacial atrophy, sequelae of radiation therapy, and many aesthetic uses such as lip and facial augmentation and wrinkle therapy. However, the limitations of fat transplantation are well known, particularly the long-term unpredictability of volume maintenance. Regenerative cell-based strategies such as those encompassing the use of stem cells hold tremendous promise for augmentation of the soft-tissue space. Preclinical studies and early clinical series show that adipose-derived stem cells offer the possibility of finally fulfilling the key principle of replacing like with like as an aesthetic filler, without the drawbacks of current technology. (*Plast. Reconstr. Surg.* 118 (Suppl.): 121S, 2006.)

REGENERATIVE MEDICINE AND STEM CELLS

Regenerative medicine, broadly speaking, refers to the use of the body's raw materials of repair—namely, cells, matrix, and/or chemical compounds—to naturally restore appearance or function. This strategy applies equally to both life-threatening diseases such as heart attack and cosmetic and reconstructive indications. In many respects, cells are the most critical and elusive members of the "regenerative triad." Cells, unlike many matrix macromolecules, proteins, and small molecules, cannot be manufactured per se. They must be harvested, purified, and in most cases replicated before clinical use. Furthermore, this process must be performed in a manner such that the therapeutic potential of the cells is not dissipated or removed altogether.

Stem cells have received significant attention as an ideal source of regenerative-capable cells because of their multipotentiality and ability to replicate. Furthermore, stem cells have been used in a limited fashion for decades with great clinical success. For example, stem cells from the bone marrow, peripheral blood, and even umbilical cord blood have been used to treat a variety of diseases.[1,2]

Although stem cell therapies can be used allogeneically, the issue of transplant-related immune responses, however, limits the universal applicability of allogenic cell treatments and stem cell therapies.[3] The innate problems associated with allogenic stem cell transplantation such as host immune responses and implant rejection can be avoided by the use of autologous stem cells. Furthermore, autologous stem cells, such as those derived from bone marrow or adipose tissue, can be used clinically for regenerative cell therapy only if they can be obtained in sufficient quantities. Adipose-derived stem cells can be easily processed from lipoaspirated fat and can provide the physician with a significant quantity of multipotent stem cells for a variety of therapeutic regenerative medicine therapies.

A BRIEF BACKGROUND OF FILLER MATERIALS

The need for fillers to "replace like with like" is found in over a century's experience with both

From the Department of Research and Technology, Division of Biologics, Cytori Therapeutics, Inc., and Department of Surgery, Division of Plastic Surgery, University of California, Los Angeles.
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DOI: 10.1097/01.prs.0000234609.74811.2e

Adipose-derived stem and progenitor cells have not been approved for use by the FDA.

Prolipostem: scientific study

Adipose-Derived Stem Cells and Their Secretory Factors as a Promising Therapy for Skin Aging

BYUNG-SOON PARK, MD, PHD,[*,†] KYOUNG AE JANG, MD,[†] JONG-HYUK SUNG, PHD,[*]
JEONG-SOO PARK, PHD,[‡] YONG HYUN KWON, MD,[§] KEA JEONG KIM, MD, PHD,[§] AND
WON-SERK KIM, MD, PHD[§]

BACKGROUND Adipose-derived stem cells (ADSCs) and their secretory factors can stimulate collagen synthesis and migration of fibroblasts during the wound healing process. Conventional treatments for skin aging, such as lasers and topical regimens, induce new collagen synthesis via activation of dermal fibroblasts or growth factors. Considering the results of our previous study, ADSCs can also be used for the treatment of skin aging.

OBJECTIVE The aim was to verify the effectiveness of ADSCs for the treatment of skin aging.

METHODS We analyzed secretory factors of ADSCs and intradermally injected ADSCs (1×10^6 cells in 1 mL of Hanks' buffered salt solution) and conditioned media of ADSCs on the back of a micropig. In addition, as a pilot study, intradermal injections of purified autologous processed lipoaspirate (PLA) cells were tried with the photoaged skin of one patient.

RESULTS We demonstrated that ADSCs produce many useful growth factors, increase collagen production in animal study, and reverse skin aging in human trial.

CONCLUSION ADSCs and their secretory factors show promise for application in cosmetic dermatology, especially in the treatment of skin aging.

The authors have indicated no significant interest with commercial supporters.

The concept of regenerative medicine, using the body's own stem cells and growth factors to repair tissue, is an alternative therapeutic strategy for damaged tissue repair and is becoming a major candidate for cell therapy.[1] Adipose-derived stem cells (ADSCs) are pluripotent mesenchymal stem cells, which have characteristics similar to bone marrow–derived mesenchymal stem cells. In addition, compared with bone marrow–derived mesenchymal stem cells, ADSCs can be acquired in large quantities with a simple surgical procedure.[2] There have been many clinical applications for mesenchymal stem cells, including ADSCs for compensation of skin defects and wound healing.[3–5] In a previous study, our group demonstrated that ADSCs, and conditioned media of ADSCs (ADSC-CM), stimulated collagen synthesis and migration of fibroblasts during the wound healing process. These results may be associated with numerous other factors produced by ADSCs (accepted by the *Journal of Dermatologic Science*). Conventional treatments for skin aging, such as laser and topical regimens, induce new collagen synthesis via activation of dermal fibroblasts or growth factors.[6] Considering the results of our previous study, ADSCs can also be used for the treatment of skin aging.[5] To verify this, we conducted in vitro and in vivo animal studies, including a pilot study using volunteer and fresh autologous ADSCs.

For the in vitro study, adipose tissue samples were obtained through elective liposuction with informed consent. After isolation of the ADSCs, as mentioned in many previous reports, we depicted ADSCs by

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Adipose-derived Stem Cell Current Findings and Future Perspectives

Adipose-derived Stem Cells: Current Findings and Future Perspectives

Published on February 23, 2011

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Abstract: Adipose tissue is an abundant source of mesenchymal stem cells, which have shown promise in the field of regenerative medicine. Furthermore, these cells can be readily harvested in large numbers with low donor-site morbidity. During the past decade, numerous studies have provided preclinical data on the safety and efficacy of adipose-derived stem cells, supporting the use of these cells in future clinical applications. Various clinical trials have shown the regenerative capability of adipose-derived stem cells in subspecialties of medical fields such as plastic surgery, orthopedic surgery, oral and maxillofacial surgery, and cardiac surgery. In addition, a great deal of knowledge concerning the harvesting, characterization, and culture of adipose-derived stem cells has been reported. This review will summarize data from *in vitro* studies, pre-clinical animal models, and recent clinical trials concerning the use of adipose-derived stem cells in regenerative medicine.

Aesth Plast Surg
DOI 10.1007/s00266-011-9716-x

ORIGINAL ARTICLE

Staged Stem Cell-enriched Tissue (SET) Injections for Soft Tissue Augmentation in Hostile Recipient Areas: A Preliminary Report

Tunc Tiryaki · Necati Findikli · Demir Tiryaki

Received: 25 October 2010 / Accepted: 18 March 2011

Abstract
Background Autologous fat transplantation is frequently used for a variety of cosmetic treatments and difficult reconstructive indications such as involutional disorders, hemifacial atrophy, sequelae of radiation therapy, or similar problems. However, the limitations of fat transplantation are well known in such difficult cases, particularly the long-term unpredictability of volume maintenance. The ideal method of preparing autologous fat grafts optimizes tissue survival and reduces the variability of outcomes. We propose that enriching traditionally prepared fat grafts with adipose-derived regenerative cells (ADRCs) represents one such method.
Methods Using a staged approach, we performed cell-enriched fat transfer by injecting autologous ADRCs into soft tissue that was recently grafted using traditional methods of fat transfer. Over a 3-year period, data were prospectively collected from 29 patients who underwent a single session of stem cell-enriched tissue injections (SET).
Results Cell-enriched grafts ranged in volume from 10 to 390 cc per recipient area and were obtained by manual or automated processes. The mean follow-up period was 10 months. Postoperative atrophy of the injected tissue was minimal and subjectively did not change after 8 weeks. Of note, historically reported rates of atrophy range from 20 to 80%. All patients were satisfied with the primary result with no need for a secondary session except for the cosmetic cases.
Conclusion These preliminary results suggest that SET is safe and may provide superior results compared to traditional fat grafting. By performing the procedure in a staged approach, operating room expenses are minimized, which ultimately decreases the cost of the procedure. Adipose-derived regenerative cells may mitigate early ischemia by increasing angiogenesis, decreasing apoptosis, and modulating the local inflammatory response. This technique may be of particular value to the surgeon when grafting high volumes of fat or when faced with hostile recipient area conditions, including fibrosis and post radiation.

Keywords Stem cells · Plastic surgery · SET · Hostile recipient area · Lipoinjection · Tissue engineering · Fat transplantation · Adipose-derived stem cells

Introduction

A Comparison of Cell-Enriched Fat Transfer to Conventional Fat Grafting after Aesthetic Procedures Using a Patient Satisfaction Survey

Brian Mailey, MD, Salim Saba, MD,* Jennifer Baker, MD,* Christopher Tokin, MD,* Sean Hickey, MD,* Ryan Wong, MD,* Anne M. Wallace, MD,* and Steven R. Cohen, MD*†*

Introduction: The role of regenerative cells in adult human fat is still unfolding. At present, limited clinical studies comparing patient satisfaction with cell-enriched fat transfer (CEFT) to conventional autologous fat transfer (AFT) for aesthetic indications have been performed. Herein, we present our data obtained from patient satisfaction questionnaires.

Methods: Patients undergoing fat grafting received AFT or CEFT. Study participants were surveyed for overall satisfaction, symmetry, deformity, scarring, and pigmentation. Hospital charts were reviewed for complications, and patient survey responses between the groups were compared.

Results: Between January 2009 and September 2011, 36 patients had 6-months follow-up and were mailed surveys. Of these, 17 (12 CEFT and 5 AFT) returned completed *Patient Satisfaction Rating* surveys. At a median follow-up time of 10.7 months, the overall mean satisfaction rate was 5.2 of 6 (5.3 vs 5.0 for CEFT and AFT, respectively, $P = 0.42$). There were no significant differences about deformity (5.1 vs 4.7, $P = 0.50$), symmetry (4.5 vs 5.0, $P = 0.48$), or scarring (5.3 vs 4.5, $P = 0.23$). However, pigmentation was improved in the CEFT vs the AFT groups ($P < 0.001$). No patients in the AFT group noted skin pigmentation improvement, whereas 7 of 12 receiving CEFT noted improvement in skin pigmentation.

Conclusions: Cell-enriched fat transfer to the face and body of aesthetic patients produces high satisfaction rates. Our preliminary data demonstrates similar satisfaction with regard to symmetry, scarring, and deformity in patients treated with CEFT versus AFT, without any complications. Unexpectedly, a clinical and statistical improvement in pigmentation was seen for patients treated with CEFT over AFT. Further studies need to be done to better understand this phenomenon.

Key Words: fat graft, regenerative cell, stem cell, patient survey, pigmentation, patient satisfaction

(*Ann Plast Surg* 2013;70: 410–415)

Autologous fat grafting for recontouring soft tissue defects began surging in popularity in the 1980s.[1,2] Early experiences focused on craniofacial soft tissue augmentation[3]; however, reconstructive surgeons quickly expanded applications of autologous fat transfer (AFT) to include reconstruction of congenital anomalies, traumatic sequelae, and oncologic resections.[4–9] Aesthetic surgeons have also used fat as an injectable for soft tissue rejuvenation.[10] Inherent properties of fat, namely, safety, technical ease, autologous nature, and possibility of altering outcomes by repeat intervention make it an ideal material for reconstruction. Despite excellent immediate results, traditional fat-filling procedures claim inconsistent long-term durability with up to 70% of the initially implanted tissue volume reabsorbed.[11,12]

We now know that aspirated adipose tissue consists of 2 components, namely, lipid inclusion containing adipocytes and stromal cells containing a cellular compartment.[13] Recently, these inherent properties of the preinjected fat have been proposed as the explanation for differences in final graft survival.[14–16] In 2001, the existence of multilineage regenerative cells in adult human fat was recognized and published by Zuk et al.[17,18] These regenerative cells maintain the ability to undergo cellular differentiation and regeneration.[13] In particular, adipose-derived regenerative cells (ADRCs) have the potential to differentiate into tissue types of mesenchymal origin, namely, adipocytes, chondrocytes, osteoblasts, and myoblasts, depending on environmental influences.[19] The therapeutic potential of these multipotent cells have become of basic interest to many disparate specialties of medicine and may be the explanation for variable fat graft survival. Comparison of whole fat to lipoaspirated fat noted whole fat contained twice the number of progenitor cells.[20] These results were explained 2-fold. First, ADRCs are primarily located around large vessels, which are mostly left at the donor site during traditional liposuction. Second, some ADRCs are released into the supernatant portion of the liposuction aspirates and discarded. These important findings offer additional insight into harvest and preparation of fat grafts, and potentially support the use of lipoaspirated fat enriched with ADRC.

Other promising features of fat grafting have recently been recognized. These include an increase in vascularity caused by proangiogenic factors and dermal regeneration.[21] The inherent properties of preinjected fat (ie, adipocyte maturity, extracellular scaffold, and presence of ADRC) may explain theses differences in fat graft behavior.[14,15] The emergence of commercially available devices to enrich preinjected fat with autologous ADRC has introduced a practical way of incorporating regenerative cells into clinical practice. Similar to many new technologies, regenerative cell-enriched fat has been received with both promise and skepticism. To decipher the degree of true science versus marketing-hype, several authors have reported their clinical and preclinical data. Most of the reports have been promising,[20–22] but additional work is still needed before a consensus and exact utility for the cells can be reached. In our practice, we have offered patients undergoing fat transfer to have their fat enriched with autologous ADRC before injection since 2009. During the past 2 years, our experience using this method has been positive from both investigators and patients. The purpose of the current study was to determine and compare patient satisfaction scores in all patients undergoing fat grafting, using either the conventional, standard AFT method or a cell-enriched fat transfer (CEFT). This was conducted using a patient satisfaction survey questionnaire. We also reviewed patient charts for any systemic or

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From the *Division of Plastic Surgery, School of Medicine, University of California San Diego; and †Faces+, San Diego, CA.
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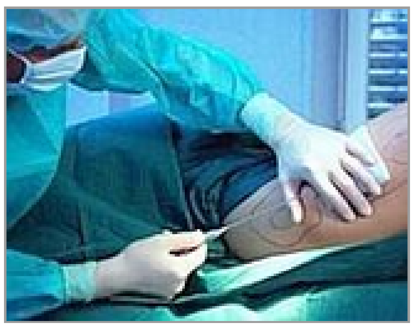
Staminali pluripotenti nel grasso prelevato con la liposuzione

Gli studiosi hanno trovato delle cellule chiamate «Muse-At» capaci di resistere in condizioni eccezionali di stress



MILANO - Da grasso prelevato con gli interventi di liposuzione a cellule staminali jolly, potenzialmente in grado di trasformarsi in qualsiasi tessuto del corpo, e "highlander", capaci cioè di