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BioMediTech

# Bioactive Glass Ions as Inducers of Osteogenic Differentiation of the Human Adipose Stem Cells

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# BioMediTech

Joint institute of University of Tampere & Tampere University of Technology

Over 250 scientists in basic and translational research



- Tissue engineering and stem cell technology
- Biomaterials
- Sensor and actuator technologies
- Measurement and imaging technologies
- Biotechnology
- Immunology
- Cancer and mitochondrial research
- Systems biology
- Bioinformatics
- Computational methods in biomedicine



## Adult Stem Cell Group UTA



#### Group leader PhD, Adj.Prof. Susanna Miettinen Expertise

- Adipose stem cells, Mesenchymal stem cells, Dental stem cells
- Osteogenic, adipogenic and chondrogenic differentiation
- Translational research
  - Culture conditions of stem cells for clinical use
    - Animal derived material free work flow
  - Clinical cell therapy
    - Regulatory issues (with Regea Cell Center and Tissue Bank)
    - •Bone defects in cranio-maxillofacial area

#### **Basic research**

- Characterization of stem cells
- Bone tissue engineering
  - Biomaterials, growth factors
  - Cell signaling and differentiation
  - Stem cells and immunology

#### **Research interests**

- Angiogenesis & bone
- Mechanical and electrical stimulation and differentiation

#### Group

- 4 post docs
- 9 PhD students
- 2 undergraduate students
- 3 technicians

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### **Clinical cases with autologous ASCs**

- Bone defects in cranio- maxillofacial area
- First clinical cases
  - November 2006
    - Ossification of frontal sinus
- Over 23 patients treated
  - 5 cranial defects
  - 4 frontal sinus ossifications

#### 14 maxillar/mandibular defects

- ossification on defect site
  OR ossification in well vascularized site
- ± rhBMP-2
- biomaterials β-TCP or BaG
- Encouraging results







## Motivation

- Human adipose stem cells (hASCs) are an excellent cell type for e.g. bone tissue engineering
  - Easy isolation, high yield, multipotency, autologous or allogenous etc.

Osteogenic differentiation

- Considering clinical applications, <u>the osteogenic differentiation</u> of hASCs needs to be fast and effective
  - → current methods do not fulfill this requirement
- → More efficient methods are urgently needed





# Aims

 Do cells require surface contact or are the dissolved ions enough to induce osteogenesis?
 Are osteogenic supplements required in addition to BaG ions?
 Are there differences between the different BaG compositions?





# Our approach

**Bioactive glass compositions.** The glasses were processed into granules of

size 0.5-1.0 mm.

		wt-%										
		Na <sub>2</sub> O	K <sub>2</sub> O	MgO	CaO	$P_2O_5$	B <sub>2</sub> O <sub>3</sub>	SiO <sub>2</sub>				
1	S53P4	23.0	0.0	0.0	20.0	4.0	0.0	53.0				
	1-06	5.9	12.0	5.3	22.6	4.0	0.2	50.0				
	2-06	12.1	14.0	0.0	19.8	2.5	1.6	50.0				
	3-06	24.6	0.0	0.0	21.6	2.5	1.6	50.0				

## The effect of BaG extracts on:

hASC viability



*BM = basic medium, OM = osteogenic medium, hASC = human adipose stem cell* 



#### Cell viability and proliferation



- Cells stay viable in all the extracts for the whole culturing period (14d)
- At 14d 1-06, 2-06 and 3-06 BM extracts increase proliferation
- At 14d all the four OM extracts decrease proliferation



#### BioMediTech Institute of Biosciences and Medical Technology Osteogenic marker gene expression



• The expression of DLX5 and OSTERIX was increased in all the four OM extracts at 14d

![](_page_9_Picture_0.jpeg)

# Mineralization

![](_page_9_Figure_2.jpeg)

- All the four OM extracts induced a high amount of mineral formation already at 14d time point
- explains the reduction in cell amounts

![](_page_10_Picture_0.jpeg)

## Mineralization

![](_page_10_Figure_2.jpeg)

Raman analysis confirmed the result of Alizarin red S staining: all the four OM extract treated samples contained calcium phosphate mineral, which was not detected in control OM

![](_page_11_Picture_0.jpeg)

## Collagen-I amount and localization

## Collagen-I Actin cytoskeleton Nuclei 13d

![](_page_11_Figure_3.jpeg)

- In control OM collagen-I still inside the cells
- In extract OMs cells have secreted the collagen-I into the ECM Ojan

![](_page_12_Picture_0.jpeg)

## Osteocalcin amount and localization

### **Osteocalcin Nuclei 13d**

![](_page_12_Figure_3.jpeg)

# All the OM extracts increase osteocalcin production to the ECM.

![](_page_13_Picture_0.jpeg)

# Conclusions

- All the OM extracts induced exceptionally fast and extensive osteogenesis of hASCs compared to the OM control.
- BM extracts could not induce the osteogenesis of hASCs → traditional OM supplements required in addition to the BaG ions.
- Of the studied extracts, 2-06 and 3-06 OM turned out to be the best inducers of osteogenesis → The extract from these two contained the highest concentrations of <u>calcium</u> and traces of <u>boron</u>.
- The excellent performance of all the OM extracts encourages to utilize them in bone tissue engineering applications as effective inducers of osteogenesis

Ion concentrations of the BaG extracts (mg/kg). Analyzed by ICP-OES (inductively coupled plasma optical emission spectrometer).

	Са	к	Mg	Р	Si	Na	В
DMEM/F-12	41	173	18	30	<loq< th=""><th>3480</th><th><loq< th=""></loq<></th></loq<>	3480	<loq< th=""></loq<>
S53P4	115	180	16	<loq< th=""><th>61</th><th>3760</th><th><loq< th=""></loq<></th></loq<>	61	3760	<loq< th=""></loq<>
2-06	153	360	16	<loq< th=""><th>53</th><th>3730</th><th>3.4</th></loq<>	53	3730	3.4
1-06	116	243	40	21	52	3620	<loq< th=""></loq<>
3-06	131	172	16	<loq< th=""><th>56</th><th>3750</th><th>2.6</th></loq<>	56	3750	2.6

![](_page_14_Picture_0.jpeg)

# **Collaboration & Funding**

#### Collaboration

- Åbo Akademi University
  - Professor Leena Hupa
  - MSc Leena Björkvik
  - University of Jyväskylä
    - Professor Janne Ihalainen
    - Dr. Heikki Häkkänen

#### Tampere University of Technology

- **Professor Minna Kellomäki**
- University of Tampere
  - Dr. Reija Autio

#### **Funding**

- **TEKES Human** Spare Parts project
- Doctoral Programme in Biomedicine and Biotechnology
- Pirkanmaa Hospital District Science Centre
- Finnish Concordia Fund

![](_page_14_Picture_18.jpeg)

![](_page_14_Picture_19.jpeg)

Åbo Akademi

UNIVERSITY OF TAMPERE AMPERE UNIVERSITY OF TECHNOLOGY

Tekes

Elämän

ähden

![](_page_15_Picture_0.jpeg)

## Adult stem cell group

![](_page_15_Picture_2.jpeg)

### <u>Group leader</u>

#### **PhDs**

Susanna Miettine<mark>n</mark>

Sari Vanhatupa

Mimmi Patrikoski Laura Kyllönen Nick Walters

#### PhD students

Panu NordbackAnnukka VuorinenMiina OjansivuLaura HyväriSanna PitkänenKaisa VuornosSanni VirjulaMartin WaselauKatja Ahtiainen

#### <u>MSC students</u> Laura Oksa Antonina Chouat <u>Laboratory technicians</u> Anna-Maija Honkala Miia Juntunen

Sari Kalliokoski

Thank you !

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![](_page_16_Picture_2.jpeg)

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![](_page_16_Picture_6.jpeg)

TAMPERE UNIVERSITY OF TECHNOLOGY

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![](_page_16_Picture_10.jpeg)

European Regional Development Fund