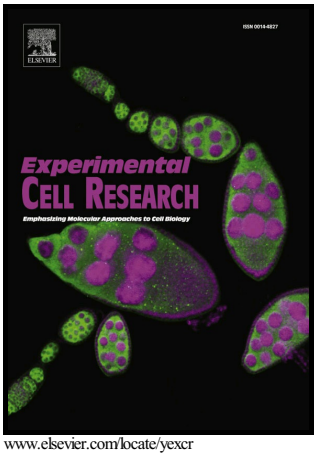

www.elsevier.com/locate/yexcr

Lab-on-a-Chip Platforms for Quantification of Multicellular Interactions in Bone Remodeling

Estee L. George, Sharon L. Truesdell, Spencer L. York, Marnie M. Saunders

PII: S0014-4827(18)30110-1
DOI: https://doi.org/10.1016/j.yexcr.2018.02.027
Reference: YEXCR10940

To appear in: *Experimental Cell Research*

Received date: 6 December 2017
Revised date: 22 February 2018
Accepted date: 23 February 2018

Cite this article as: Estee L. George, Sharon L. Truesdell, Spencer L. York and Marnie M. Saunders, Lab-on-a-Chip Platforms for Quantification of Multicellular Interactions in Bone Remodeling, *Experimental Cell Research,* https://doi.org/10.1016/j.yexcr.2018.02.027

Lab-on-a-Chip Platforms for Quantification of Multicellular Interactions in Bone Remodeling

Estee L. George[a], Sharon L. Truesdell[a], Spencer L. York[a], Marnie M. Saunders[a]

Estee L. George*, Sharon L. Truesdell, Spencer L. York, Marnie M. Saunders

[a]The University of Akron, Olson Research Center 319, 302 E. Buchtel Ave. Akron, OH, USA 44325-0302

eg55@zips.uakron.edu
slt79@zips.uakron.edu
spenceryork@gmail.com
mms129@uakron.edu

*Corresponding author

Abstract

Researchers have been using lab-on-a-chip systems to isolate factors for study, simulate laboratory analysis and model cellular, tissue and organ level processes. The technology is increasing rapidly, but the bone field has been slow to keep pace. Novel models are needed that have the power and flexibility to investigate the elegant and synchronous multicellular interactions that occur in normal bone turnover and in disease states in which remodeling is implicated. By removing temporal and spatial limitations and enabling quantification of functional outcomes, the platforms should provide unique environments that are more biomimetic than single cell type systems while minimizing complex systemic effects of *in vivo* models. This manuscript details the development and characterization of lab-on-a-chip platforms for stimulating osteocytes and quantifying bone remodeling. Our platforms provide the foundation for a model that can be used to investigate remodeling interactions as a whole or as a standard mechanotransduction tool by which isolated activity can be quantified as a function of load.

Keywords

Bone remodeling; Lab-on-a-chip; Mechanical load; Mechanotransduction; Microfluidic

1 Introduction

In the past five years, important *in vitro* studies have been performed that contribute to our understanding of osteocyte mechanotransduction—the process by which osteocytes sense mechanical load and signal to other cells to orchestrate bone remodeling. Much of this work focuses on the effects of fluid flow on osteocyte secretory factors that influence osteogenesis and bone remodeling by osteoclasts (bone resorbing cells) and osteoblasts (bone forming cells). For example, Govey *et al.* performed transcriptomic and proteomic analyses following stimulation of osteocyte-like cells with oscillating fluid flow. Importantly, chemokines *Cxc11* and *Cxcl12*—which may act as paracrine signals for the recruitment of osteoclasts and osteoblasts—were shown to be responsive to fluid flow for the first time (Govey et al., 2014). Additionally, Chen and coworkers showed fluid shear stress of osteocytes promotes osteogenic lineage commitment. After 24 h of mechanical stimulation, conditioned medium (CM) was added to mesenchymal progenitor cells. Following 24 h of exposure to the CM, DNA methylation decreased for osteogenic markers, and gene expression of later osteogenic markers increased (Chen et al., 2015). Both of these studies provide valuable information that enhances our appreciation for osteocyte signaling during mechanotransduction.

Moreover, novel techniques that model the physiological environment during mechanotransduction and subsequent bone remodeling are being devised. X. Edward Guo's group from Columbia University has focused on the development of multiscale experimental systems for the study of mechanical stimulation and associated tissue adaptation. These platforms include an *ex vivo* murine tibia model for the study of osteocyte mechanosensation and early mechanotransduction. The model incorporates a mechanical loading apparatus that delivers cyclic compressive loads to the whole bone. In this way, tissue-level stimulation can be induced and the osteocytes' early response investigated within the native environment. Another of Guo's experimental