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— Resumo dos Artigos Apresentados

8. — CONGRESSO NACIONAL — DE — BIOMECÂNICA

Unhais da Serra — Covilhã

— Resumo dos Artigos Apresentados

O documento resume os artigos do 8º Congresso Nacional de Biomecânica (CNB2019), evento que se realizou nos dias 15 e 16 de fevereiro de 2019 na unidade hoteleira H2otel, em Unhais da Serra, uma bonita e típica vila da Serra da Estrela do Concelho da Covilhã e do Distrito de Castelo Branco.
A aventura na organização destes congressos, o primeiro em forma de encontro, começou em Martinchel, Abrantes, em 2005. Esse encontro teve como objetivo primordial conhecer os investigadores que realizavam investigação na área da Biomecânica, estimular o contacto e a colaboração entre eles, promover a partilha de projetos, trabalhos e resultados, assim como revitalizar a então Sociedade Portuguesa de Biomecânica e Biomateriais, promovendo os passos necessários à constituição de uma sociedade científica de "biomecânicos", que se veio a designar oficialmente de Sociedade Portuguesa de Biomecânica (SPB) em 17 de setembro de 2009. Desde o primeiro, organizaram-se congressos em Évora (2007), Bragança (2009), Coimbra (2011), Espinho (2013), Leiria (2015) e Guimarães (2017). Procurando promover e incentivar a participação da comunidade académica, científica e técnica, no sentido de potenciar o crescimento e a intervenção da disciplina em território nacional, todos foram de sucesso científico assinalável.
É inegável que a biomecânica tem contribuído marcadamente para o alargamento das fronteiras do saber, fruto de uma investigação de excelência que tem conduzido ao desenvolvimento de projetos de investigação com relevância, entre outros, na medicina, na bioengenharia, na biologia, na automação, no desporto, na ergonomia, na reabilitação, na terapia ocupacional, no design de produtos e serviços e na ciência dos biomateriais. Este facto está bem patente nas diferenciadas ofertas educativas na área científica, no número de projetos nacionais e europeus que se têm desenvolvido, na quantidade de eventos temáticos que as instituições de ensino e de investigação vão realizando anualmente, e no número significativo de artigos publicados em importantes revistas científicas nesses diferentes domínios do conhecimento.
A organização do 8º Congresso Nacional de Biomecânica, para além de promover a apresentação e discussão dos trabalhos e potenciar desejadas relações de colaboração entre os investigadores, teve ainda como objetivo incentivar a discussão de projetos de interesse comum, assim como estreitar laços e aproximação entre investigadores portugueses e estrangeiros, em particular com os investigadores da Comunidade dos Países de Língua Portuguesa. Também temos a esperança que o congresso tenha dado um contributo importante para a sua internacionalização, reforçando os laços de colaboração com membros investigadores da International Society of Biomechanics e da European Society of Biomechanics, sociedades científicas da qual fazem parte a SPB.
Finalizamos com um sentido agradecimento a todos os membros da Comissão Científica pelo trabalho realizado na revisão dos artigos submetidos.

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Understanding mechanobiology – Linking the mechanical stimulation to cellular response

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ABSTRACT
Mechanical loading plays a crucial role throughout humans' lifetime since their embryonic development up to the tissues' homeostasis. Depending on the cell type and location, these mechanical stimuli regulate specific cell functions, namely gene expression, cell growth, differentiation and death. Cells are highly dynamic and it still remains unclear how cells sense these forces and convert them into biochemical responses. This review aims to provide an introductory research of the load-sensitive cells' mechanobiology present in the bone tissue. Subsequently, this study will contribute to design novel orthopedic implants that overcome their current impaired fixation to the natural bone.

Keywords: Mechanobiology, Mechanosensing, Mechanotransduction, Orthopedic Implants

INTRODUCTION
The human blastocyst is an early embryonic structure which contains less than 100 cells. During human's development and growth this number increases, as the reported total cell number of a human being ranges between 10^{12} and 10^{16} (Bianconi et al., 2013). Cells are constantly subjected to mechanical stimuli, both intrinsic tensions generated by active cell contraction that occur in the absence of external forces, and extrinsic shear, tensile and compressive forces applied from external loads (Vining & Mooney, 2017). The ability of cells to sense and respond to the mechanical properties of the matrix by generating forces and sensing the deformation field induced in their environment is called mechanosensing (Perrault, 2016). The mechanism through which cells convert mechanical stimuli on their environment into biochemical responses is called mechanotransduction (Humphrey, Dufresne, & Schwartz, 2014; Li, Eyckmans, & Chen, 2017; Perrault, 2016; Vining & Mooney, 2017), much faster than the chemical transduction (Perrault, 2016).
Cells' complex structure and their integration with the extracellular matrix (ECM) facilitates the mechanotransduction, for example, by the presence of glycoproteins attached on cells' surface. Among other constituents, bone tissue is composed by bone basic multicellular units including osteoblasts (bone forming cells), osteoclasts (bone resorption cells) and osteocytes (responsible for bone tissue maintenance) (Florencio-silva et al., 2015; Roseti et al., 2017). Mechanical unloading results in an unbalance between osteoclast bone resorption and osteoblast bone formation, leading to bone loss. This unloading also results in a decrease of the differentiation capacity of Mesenchymal Stem Cells (MSC) into osteoblasts (Blaber et al., 2014). Hence, mechanical stimulation at the bone-implant interface is crucial to prevent bone loss and ultimately impaired fixation of orthopedic implants (Apostu, Lucaciu, Berce, Lucaciu, & Cosma, 2017; Gasik, 2017).

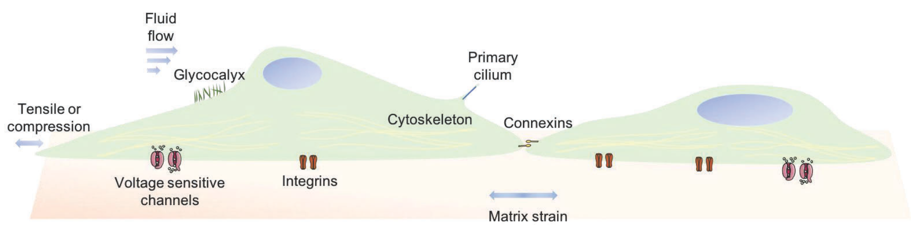

Figure 1. Intrinsic and extrinsic forces and mediators of mechanotransduction.

Cells are constantly subjected to shear flow, stretching, cyclic strain and generated tensions, where stimuli magnitude is highly dependent on the tissue itself (Uto, Tsui, Deforest, & Kim, 2017). The bone tissue is mechanically stimulated due to the gravitational forces and muscle contractions. These, in turn, result in small deformations of the tissue which generate matrix strain and interstitial flow. While the first is applied directly through the cell attachments, fluid flow is sensed through the cell membrane and both cause cell deformation (Perrault, 2016). Several cellular structures play an important role on mechanosensing, including integrins, cytoskeleton, primary cilium, glycocalyx, connexins and voltage sensitive channels, as it is represented in Figure 1.

RESULTS AND DISCUSSION

The majority of the mechanobiology studies use polymeric substrates to cultivate MSC *in vitro* which enables the manipulation of physical, chemical and biological parameters of interaction. Although it allows to investigate how mechanical forces regulate stem cell behavior, these polymeric substrates strains are far from those achieved by metallic orthopedic implants and also do not directly correlate with the microscale loading promoted on the cells (Vining & Mooney, 2017).
Overview studies on the mechanotransduction are crucial since the fundamental study on the preferred loading (type of stress, strain magnitude and frequency) would allow the design of a pro-active implant that can induce the appropriate strain (and stress) to achieve a physiological osteogenic activity.

REFERENCES

Apostu, D., Lucaciu, O., Berce, C., Lucaciu, D., & Cosma, D. (2017). Current methods of preventing aseptic loosening and improving osseointegration of titanium implants in cementless total hip arthroplasty: a review. *Journal of International Medical Research*, *0*(1–16), 030006051773269. https://doi.org/10.1177/0300060517732697

Bianconi, E., Piovesan, A., Facchin, F., Beraudi, A., Casadei, R., Frabetti, F., … Canaider, S. (2013). An estimation of the number of cells in the human body. *Annals of Human Biology*, *40*(6), 463–471. https://doi.org/10.3109/03014460.2013.807878

Blaber, E. A., Dvorochkin, N., Torres, M. L., Yousuf, R., Burns, B. P., Globus, R. K., & Almeida, E. A. C. (2014). Mechanical unloading of bone in microgravity reduces mesenchymal and hematopoietic stem cell-mediated tissue regeneration. *Stem Cell Research*, *13*(2), 181–201. https://doi.org/10.1016/J.SCR.2014.05.005

Florencio-silva, R., Rodrigues, G., Sasso-cerri, E., Simões, M. J., Cerri, P. S., & Cells, B. (2015). Biology of Bone Tissue : Structure , Function , and Factors That Influence Bone Cells. *BioMed Research International*, *2015*. https://doi.org/10.1155/2015/421746

FROST, & M., H. (1964). The Laws of Bone Structure. Springfield IL. *Charles C. Thomas*. Retrieved from https://ci.nii.ac.jp/naid/10006607916/

Gasik, M. (2017). Understanding biomaterial-tissue interface quality: combined *in vitro* evaluation. *Science and Technology of Advanced Materials*, *18*(1), 550–562. https://doi.org/10.1080/14686996.2017.1348872

Humphrey, J. D., Dufresne, E. R., & Schwartz, M. A. (2014). Mechanotransduction and extracellular matrix homeostasis. *Nature Reviews Molecular Cell Biology*, *15*(12), 802–812. https://doi.org/10.1038/nrm3896

Li, L., Eyckmans, J., & Chen, C. S. (2017). Designer biomaterials for mechanobiology. *Nature Materials*, *16*(12), 1164–1168. https://doi.org/10.1038/nmat5049

Perrault, C. M. (2016). In Vitro Bone Cell Models : impact of Fluid Shear Stress on Bone Formation. *Frontiers in Bioengineering and Biotechnology*, *4*, 1–22. https://doi.org/10.3389/fbioe.2016.00087

Roseti, L., Parisi, V., Petretta, M., Cavallo, C., Desando, G., Bartolotti, I., & Grigolo, B. (2017). Scaffolds for Bone Tissue Engineering : State of the art and new perspectives. *Materials Science & Engineering C*, *78*, 1246–1262. https://doi.org/10.1016/j.msec.2017.05.017

Rubin, C. T., & Mcleod, K. J. (1994). *Promotion of Bony Ingrowth by Frequency-Specific, Low-Amplitude Mechanical Strain. CLINICAL ORTHOPAEDICS AND RELATED RESEARCH Number* (Vol. 298). Retrieved from https://s3.amazonaws.com/academia.edu.documents/45577090/Promotion_of_bony_ingrowth_by_frequency-20160512-10590-7nopjk.pdf?AWSAccessKeyId=AKIAIWOWYYGZ2Y53UL3A&Expires=1536918110&Signature=08GMswWsggynNbf5KHejs8gfd68%3D&response-content-disposition=inline%3B filename%3DPromotion_of_Bony_Ingrowth_by_Frequency-.pdf

Uto, K., Tsui, J. H., Deforest, C. A., & Kim, D. (2017). Dynamically tunable cell culture platforms for tissue engineering and mechanobiology. *Progress in Polymer Science*, *65*, 53–82. https://doi.org/10.1016/j.progpolymsci.2016.09.004

Vining, K. H., & Mooney, D. J. (2017). Mechanical forces direct stem cell behaviour in development and regeneration. *Nature Reviews Molecular Cell Biology*, *18*(12), 728–742. https://doi.org/10.1038/nrm.2017.108