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EDITORIAL

Regeneración tisular

Los cambios en el estilo de vida y el advenimiento de conocimientos y de tecnología para el cuidado de la salud incrementaron la longevidad de las personas y los riesgos a que ellas se exponen. En la presente década, la expectativa de vida general se ubica en la octava década y en nuestro país ya supera los 70 años[1]. Si bien estas cifras son alentadoras, conllevan el aumento de riesgo de padecer patologías vinculadas con el deterioro de la condición física de los individuos.

Por otra parte, el mayor acceso a medios de transporte particular, la práctica de deportes con alto riesgo de lesiones, el sedentarismo asociado a los nuevos modelos productivos y la alta frecuencia de obesidad, originan escenarios en los que las lesiones aumentan su frecuencia y su gravedad. Es destacable mencionar que estas circunstancias no son ajenas a nuestro medio.

Desde tiempo atrás, el conocimiento de las estructuras biológicas y su dinámica, sumados al interés por conservar una buena calidad de vida, impulsó la investigación orientada a comprender y, eventualmente, aprovechar los principios de la regeneración tisular. Si observamos el número de publicaciones científicas con carácter de revisión sobre el tema, vemos que de una en 1947 [2] se alcanzó la respetable cifra de 668 revisiones en 2015, y en ese año se publicaron 3514 artículos vinculados al tema. Es particularmente revelador constatar que la base de datos PubMed recoge para 2015, 1000 registros vinculados a regeneración tisular y ósea, con notable destaque en las aplicaciones dirigidas a las correcciones dentales y cráneo-faciales.

El análisis de la regeneración tisular y, muy particularmente la ósea, se ve alimentado por el conocimiento de las características histológicas y de los mecanismos naturales de reparación[3]. A esto se fueron sumando los conocimientos de la química de la estructura mineral del hueso, el comportamiento biomecánico de sus componentes y, más recientemente, la identificación de las señales celulares que actúan en el proceso de formación y regeneración de las estructuras óseas, como las BMP (bone morphogenic proteins) y los OGP (ostegenic growth peptides), reconocidas estructural y funcionalmente en su capacidad de estimular la proliferación, diferenciación y producción enzimática y capacidad de mineralización de líneas celulares osteoblásticas[4]. La biología celular aporta el conocimiento para la obtención, implante y diferenciación de líneas celulares para su incorporación efectiva a ambientes donde su acción es requerida[5,6].

Sin embargo, las células no son suficientes en este proceso y hay esfuerzos de investigación muy diversos en lo referente a lograr construir el andamiaje (scaffold) capaz de sostenerlas. La búsqueda de matrices metálicas de titanio, los materiales de origen biológico como los derivados de colágeno, la fibroína, los alginatos, el ácido hialurónico y los derivados de quitina (quitosanos)[7-12], y los híbridos de matrices óseas libres de células con policaprolactona (DCB:PCL) capaces de sostener en el sitio apropiado las células[13], aún las de diferente origen tisular, en su sitio, constituyen un área de fuerte desarrollo experimental.

No menos importante es lograr que todo el conocimiento se traduzca en capacidad real de producir masa de material apto para la reparación deseada. En tal sentido ya se exploraron los cultivos celulares sobre matrices diversas, tanto naturales como sintéticas, la impresión en 3 dimensiones de matrices de soporte para la proliferación de células osteogénicas e incluso la producción in vivo del biomaterial de reparación en los propios sujetos receptores[14].

El avance logrado es sorprendente, sin embargo la gran mayoría de las evidencias procede de

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estudios in vitro, lo que valoriza aún más a los ensayos realizados en animales. Los ensayos clínicos, si bien limitados en la literatura, están mayoritariamente enfocados a la regeneración de material dentario o de huesos cráneo faciales y los factores que pueden favorecerlos[15, 16], lo que nos indica la necesidad de profundizar en los estudios con orientación translacional para que las soluciones con los mejores perfiles de eficacia alcancen aplicaciones clínicas a mediano plazo. Mientras tanto, la práctica médica tiene la alta responsabilidad de incidir en los grupos de mayor riesgo en la procura de la reducción de los factores prevenibles, como la obesidad, el sedentarismo y la conducción imprudente, que se asocian a patologías y lesiones cuyo tratamiento requeriría regeneración tisular.

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EDITORIAL

Tissue regeneration

Changes in lifestyle and the advent of knowledge and technology for health care increased the longevity of people and the risks to which they are exposed. In the present decade, the general life expectancy is in the eighth decade and in our country is over 70 years [(1)]. Although these figures are encouraging, they lead to an increased risk of suffering pathologies related to the deterioration of the physical condition of individuals.

On the other hand, the greater access to private means of transport, the practice of sports with high risk of injuries, the sedentary lifestyle associated to the new productive models and the high frequency of obesity, originate scenarios in which the injuries increase their frequency and gravity. It is noteworthy to mention that these circumstances are not alien to our environment.

From a long time ago, the knowledge of the biological structures and their dynamics, together with the interest in maintaining a good quality of life, stimulated the research oriented to understand and eventually to take advantage of the principles of tissue regeneration. If we look at the number of scientific publications on the subject, we can see that from one in 1947[(2)] the respectable number of 668 reviews was reached in 2015, and in that year 3,514 articles related to the topic were published. It is particularly revealing that the PubMed database collects, by 2015, 1,000 records linked to tissue and bone regeneration, with notable emphasis on applications aimed at dental and craniofacial corrections.

The analysis of tissue regeneration, and particularly bone regeneration, is supported by the knowledge of the histological characteristics and the natural mechanisms of repair[(3)]. The following mechanisms were then added to that: the knowledge of the mineral bone structure chemistry, the biomechanical behavior of its components and, more recently, the identification of cellular signals that act in the process of formation and regeneration of bone structures, such as BMP (*bone morphogenic proteins*) and OGP (*ostegenic growth peptides),* recognized structurally and functionally in their ability to stimulate proliferation, differentiation and enzymatic production and mineralization capacity of osteoblastic cell lines[(4)]. Cell biology provides the knowledge to obtain, implant and differentiate cell lines for their effective incorporation in environments where their action is required [(5,6).]

However, the cells are not sufficient in this process and there are very different research efforts regarding the construction of the scaffold capable of supporting them. The search for titanium metal matrices, materials of biological origin such as collagen derivatives, fibroin, alginates, hyaluronic acid and chitin derivatives (chitosans)[(7-12)], and extracellular bone matrix hybrids with polycaprolactone (DCB: PCL) capable of supporting cells at the appropriate site[(13)], even those of different tissue origin, constitute an area of strong experimental development.

No less important is to assure that all knowledge is translated into actual capacity to produce mass of material suitable for the desired repair. In this regard, cell cultures on various matrices, both natural and synthetic, 3-dimensional printing of support matrices for the proliferation of osteogenic cells and even the *in vivo* production of the repair biomaterial in the recipient subjects themselves were already explored.

The progress achieved is surprising, however, the vast majority of the evidence comes from *in vitro* studies, which further enhances animal testing. Clinical trials, although limited in the literature, are mostly focused on the regeneration of dental material or facial skull bones and the factors that may favor them[(15, 16)], which indicates the need to deepen studies with translational orientation so that the

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solutions with the best profiles of effectiveness reach clinical applications in the medium term. In the meantime, medical practice has a high responsibility to influence the groups at greatest risk in order to reduce preventable factors, such as obesity, sedentary lifestyle and reckless driving, which are associated with pathologies and injuries whose treatment would require tissue regeneration.

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