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Editorial

Bone Tissue Engineering: Problems Facing a Bench-Side to Bedside Solution

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The field of tissue engineering has expanded at a staggering rate. In terms of bone tissue engineering research alone this has been represented by a dozen or so manuscripts being published in 1990, increasing to almost 18,000 at the time of writing. This is compounded by the fact that the tissue engineering market is estimated to be approximately 90 billion USD by 2016 [1]. Even so, the leap from research to a reliable commercial product in bone tissue engineering has been slow to say the least, specifically in terms of bioactive materials. This begs the question: What factor(s) are contributing to this evident gap between science and clinics? Does the majority of burden lay with us the scientists? Are clinicians significantly invested in progress? Are the regulatory bodies actively inhibiting progress? Are the industrial targets pulling their weight? And finally, are our funding bodies sufficiently versed in 'the clinical problem' to fairly assess true translational medicine? The truth would appear to suggest that all stakeholders have questions to answer.

In terms of the current state of the art of bone tissue engineering, basic research has lead the way. Cell free and cell seeded scaffolds in both degradable and non-degradable options have been devised [2-6]. Protein releasing scaffolds have all been actively pursued in an attempt to provide biological 'kick-start' cues to promote tissue regeneration [7-9]. Consequently, multiphase scaffolds that can potentially co-inhabit single or several cell types as well as releasing growth factors in a variety of release profiles have emerged as the next generation bioactive scaffold [10,11]. It would be wrong to say that the field hasn't produced fascinating and promising results, as well as demonstrating the intense biological and engineering talent within the field. But have we digressed? Are we unwittingly distracted by 'sexy' science and consequently have pushed the goal of getting a product to clinics to the long arm? The idea of a 'smart' scaffold that provides osteoinductive and conductive elements in terms of surface properties and temporal growth factor(s) release is incredibly attractive to recapitulate the natural events of bone healing. However, in all honestly, would such a product be commercially viable or will our mammoth research achievements end up with a price tag that will see it shelved before we can bask in our clinical success?

One could tentatively suggest that we have taken the 'easy' route to tackling bone regeneration from a research perspective. For instance, recent advancements in technology have seen a myriad of scaffold choices emerging [12]. In contrast, little is invested in discriminating the pathophysiology of the condition that causes non-unions and other conditions which ultimately require bone regeneration approaches [13,14]. If more was delineated about the underlying condition our biological approach to regenerative medicine would become more empirical compared to the current lack of consensus on what factor to use, when and at what effective dose. Realistically, it will take a converging and comparable effort on the biological and engineering fronts to address this.

Another clear hurdle in getting a product to market is attracting key industrial partners. Given the huge cost associated with the inevitable clinical trial(s) it is not surprising that companies carefully and diligently chose their partners. It is this marriage that will effectively deflect funds from other projects and therefore, requires a business as well as a scientific decision. Interestingly, practically all existing clinical trials relating to bone regeneration and scaffolds are focused on temporomandibular and dental applications [15]. One could argue that challenges of a high load bearing region with a significant defect is reduced in these applications, thereby increasing chances of success. That is not to say that these clinical problems do not require addressing. However, the lack of progress within long bone defect applications speaks volumes to the challenges we face in the field both from a basic science and commercial perspective. Rather it would suggest that, with some exceptions, current modalities in long bone defects pose too much of a financial risk for the relevant industrial partners to take.

The term 'translational medicine' is often used in the context of tissue engineering generally. This poses another challenge for bone tissue engineering. This may partly be because there is a lack of consensus or rather differing definitions between scientists, clinicians and funding agencies as to its meaning. Part of the solution to this may be to incorporate more research focused orthopaedic surgeons into the peer reviewing grant system as well as on the steering committees within the agencies

themselves. Consequently, this may provide a balanced and pragmatic system of selecting true translational proposals that have a realistic opportunity for addressing a real clinical problem. Indeed, if the systems were more transparent it would be also beneficial to include industrial representatives on committees to help steer the funding bodies towards effective research. Taking this notion a step further, the eagerness of the funding agencies to fund 'translational medicine' should not overcast the importance of basic science and its contribution to translational approaches that arise from such research.

So, reflecting back on the initial question relating to the main contributors to the slow progress of bench-side to bedside bone tissue engineering, it seems that all stakeholders have some responsibility to bear. It is likely that when the dust settles and the 'sexy science' is evaluated in terms of commercial viability, we may find ourselves re-tracing our steps to produce a comparably simplified scaffold. Also, from a regulatory stand-point, cell-free scaffolds will potentially prove the most commercially and clinically viable pursuit. One thing seems abundantly clear, however; only a collaborative effort will eventually make the progress required in realising a bench-side to bedside product that will effectively help the millions of patients world-wide that await such a treatment.

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