Extreme Tissue Engineering

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Extreme Tissue Engineering

Concepts and Strategies for Tissue Fabrication

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Preface: Extreme Tissue Engineering – a User's Guide

The most important first task of any User's Guide is to dispel possible misconceptions of what the 'user' might reasonably expect. In this case, there can be a small ambiguity in the title for those who are unfamiliar with 'tissue engineering'. So, if you are skimming through this book, expecting to learn how you could engineer extreme (or *weird*) tissues, it is recommended that you pop it back on the shelf and move to the science fiction movie section. On the other hand, if you want to learn how emerging concepts and strategies might be blended to revolutionize how we engineer (very familiar) tissues, then read on.

This is an unusual textbook in a field rich in books which come from the many sectors of activity which make up 'tissue engineering'. It is different, not least, because it tries to integrate these diverse viewpoints, rather than giving just one perspective. This tends to set it apart because of things that it is *not*. It does *not* come from the direction of explaining *specific* technologies or particularly useful cell types. Neither does it aim to describe *specific* control mechanisms or *target* tissue applications. The logic here is that there are far too many applications, body sites and permutations to treat them all in just a few hundred pages (and there are already many thousands of written pages out there anyway). It is also *not* a multi-author book, with single, specialist, research-level chapters.

It *does* seem to be unique in the field, as a single-author, basic textbook of advanced tissue engineering concepts, across disciplines. It *does* aim to enable newcomers (or the puzzled-but-interested) to understand much better what that mass of facts and data out there might really mean. First, though, it aims to provide a unified introduction, whether your original training is in cell biology, engineering, biomaterials, surgery or other contributing specialities.

It is illuminating to ask why, in two decades, there have been so few (if any) basic-concept texts, especially as the underlying idea *seems* to be so simple. Understanding this (discussed at length in Chapter 1) begins to explain what makes tissue engineering so *special* and, indeed, *illusive*. The answer is grounded in its position at the touch-and-merge point of so many well established disciplines.

It is arguable that tissue engineering barely exists unless its activity includes some form of integration or merger of ideas from two or more of its more established component subjects. These 'components' include cell biology, materials science, surgery or sensor biophysics, protein chemistry and bioreactor technology, to name a few. If this is true, then we cannot avoid the logic that the work we do in this subject overlap zone called tissue engineering, *must* be *integrated* or *merged*. We cannot claim that our new hybrid subject is generating real synergies if we work away at cell biology in January, materials science in February and surgical science in March, etc.

Worse still, it has proved all too easy to toil deeply within one of the single-component disciplines to solve questions which, in the end, have little logical value when applied outside that discipline. Imagine, for example, how far sustainable cities would be advanced if the Norwegian civil engineers developed new insulation for homes in Oslo with the aim of linking this with findings from the Turkish seismic geologists on tectonic plate movements around Istanbul. **If we claim to generate synergies between disciplines, deep integration is an essential**.

By analogy, those of you who have experienced the London public transport system in a hot summer rush hour will understand more clearly the critical

importance of the 2–3 mm that separate 'close' from 'touching'. Arguably, the social, legal and emotional effects of being tightly squeezed into physical contact on the 6:00 pm Victoria Line tube in Central London are similar to those where academic disciplines merge at their edges. **Both events have more to do with anxiety and imagination than subject-matter or cold logic**.

This is why a complete chapter is dedicated to exploring what tissue engineering actually *is*, and where it originates. After all, if you *must* grapple with the Victoria Line tube, it is good to know about your fellow travellers.

The core trouble is that the tissue engineering 'concept' is, in effect, based on combinations of knowledge packets which are drawn from the simpler parts of its component disciplines. As a result, it is terminally tricky in tissue engineering to explain the *same*, very *basic* topics to individuals who have had a wide range of specialist training, for the simple reason that, at any one time, one or more sets of your readers will almost certainly become seriously bored. For example, where the text explains the basic concepts of one contributing discipline (e.g. cell culture, aimed at engineers, or stress-strain measurement to biologists) it becomes laughably simple – and terminally boring – for the expert group. However, leaving out any of these basic parts immediately compromises our aim of a single, *integrated* set of concepts (and we have already glimpsed the importance of integration).

Consequently, it is almost *guaranteed* that some readers will be bored (while others are learning) – and this is a seriously *undesirable* publication plan. Suddenly, it is easy to understand how we reach our present position of having a plethora of focused, specialist texts. Yet there is clearly a broad need for just such a 'doomed' textbook, explaining and integrating the basic concepts. Is it too high a hurdle, then, to explain the concepts and strategies of tissue engineering in an integrated, joined-up manner? Certainly, it would be helpful to students trying to understand the strategies and logics behind more specialist applications, such as engineering cartilage, nerves or blood vessels, **whatever sector they were trained in**.

But there is a way around this difficulty. The style of *Extreme Tissue Engineering* is designed to entertain and excite *all* reader groups, whether they are being (re-)introduced to their own discipline or to a new one. After all, if the claims of tissue engineering enthusiasts are even half true, there should be plenty of excitement to draw on at the various discipline interfaces. One way of generating engagement, and incidentally of helping with the learning process, is to use amusing, unusual analogies and extreme (even ridiculous) examples.

Extreme Tissue Engineering adopts this approach. It aims to *integrate* concepts from each of the component fields, often pulling together pairs of traditionally distinct subjects. At the same time, it actively approaches topics from new angles, drawing its logic threads from colourful starting points and illustrating this with recurring analogies. Wherever possible, these analogies bring to life abstract concepts by drawing on the everyday human world and its artefacts, or on familiar animals and plants. All of this allows us to understand tissue engineering from new perspectives (hopefully tracking where it is going) and why it must become *extreme* to get there. Indeed, the very process of producing a coherent explanation for tissue engineering logic inevitably highlights its paradoxes and identifies questionable assumptions.

On some occasions, these illustrative analogies help us to see the inherent flaws in current strategies. In others, they point us towards possible solutions. In all cases, their aim is to stimulate your own ideas on the problem and to cement the issues in your memory. First and foremost, it should be fun, refreshing and easy to remember.

But this all leads to a rather distinctive, even unfamiliar style. It really should generate controversy in areas where concepts and approaches are deep-rooted. For this reason, it is important that discussions around the logic and content are separated from reaction to its style, which is just a necessary tool for engagement. Where it makes our field easier to understand and explain, especially to newcomers, it may make a significant long-term contribution. If and when it successfully challenges or redirects worn and suspect strategies, it will have performed

Text Box 1 Author's personal note

I recently spoke at the Cheltenham National Science Festival to an enthusiastic lay audience. They were keen to hear about how tissue engineering and regenerative medicine *could* help in the health of ordinary people. Once our small panel had finished its story of enthusiasm and promise, we took questions. As many of us have found before, these questions were poignant and hit at the nub of chronic health problems, which we still tend to skirt around or back away from. Gradually, it became clear that some members of the audience were themselves threatened or were caring for treasured spouses, parents or birth-damaged children.

These are the real issues we must have in mind as we set loose our personal optimisms on a desperate world. We *must* be sure we can deliver before we speak – and not just under the 'scientific-eventually' caveat. Equally, it clearly becomes our duty, once we speak of these aims, to deliver to the very best *intellectual* level we can. In the face of false hopes offered to the mother of a damaged child, it is not enough only to point to long hours in the lab and a healthy grant income. Only extremely clear, joined-up thinking will do.

a more immediately useful role. Clearly, both objectives must be good for a subject as new and uncertain as tissue engineering. This is especially true where our list of success stories is so modest – and so impatiently awaited (see Text Box 1).

In short, this book is designed to leave you with an in-depth understanding of the overriding questions and problems of tissue engineering. As a bonus, you may also discover a selection of the possible solutions and routes to reach our tissue goals. It should transform how you see the rest of tissue engineering. In particular, it should make it easier for newcomers to understand and interpret the rich collection of specialist textbooks already produced by the many tribes of tissue engineering.

There is a liberal use of text boxes and footnotes throughout. These are included as 'asides' and caveats, designed to colour and enrich the logic without deflecting the reader from its main track (for example, see Text Box 1 above). Where these are successful, they will make it easier to follow the thread and to remember its key points.

In places, there are simple questions aiming to draw your thinking to new places after you have put the book down. These are designed not for repetition of message, nor to save your professors work; rather, they give you a chance to carry on with or extend the concept on the train going home, or when you are out enjoying the park. There are many sectional and chapter summaries which should allow you to recap on the main points at regular intervals and understand better where they are leading us.

Through the length and breadth of the book, you will find examples and analogies. Some are designed to inform, some to bring an idea or concept to life – even where it is not your favourite topic. Yet others are just embarrassing, even silly, as such images are perhaps the most effective way to lodge ideas and facts in the mind. An example of this mnemonic effect can be found in a highly successful UK/European advert series for car insurance. Clearly, insurance is one of the more challenging products when advertisers are required to generate 'customer excitement' or 'brand identity'.

For example, those of you who have experienced one recent campaign will now be deeply imprinted with a completely abnormal image-association based on the word '**meerkat**'.[1] You will almost certainly recall an image of fluffy Russian-accented puppets angry at a car insurance company for stealing their website name. Clearly, before this rather silly series of ideas were imprinted, the word would have brought to mind a more realistic image of jerky, mongoose-like mammals, sitting tall in the African veldt (if it is not shown in your area, you can get the gist from the campaign's website: www.comparethemeerkat.com).

Tissue engineering is too young to be brittle, and too much in need of successful translations to be

[1] You have just experienced an example of the very illustration under discussion. Hopefully, this circle-within-a-circle helps you to appreciate how potent these illustrations can be in leaving recallable ideas in our minds.

strategically fixed. The term 'extreme tissue engineering', then, has been coined here to reflect the target of generating a distinctive and challenging new approach. Its focus and reason for extremeness is the inescapable need for cross-discipline integration. This is an integration based on balance and equal voice, rather than a spurious democracy linked to the perceived 'size' of a contributing discipline. The number of workers in a discipline, or grants awarded to it, correlates depressingly badly with its success in solving the big problems of society. 'Integrations' which resemble the merger of shrimp and basking shark are not helpful to our cause. The trouble is, it is perfectly possible that the 'shrimp' (i.e. the minor discipline) might have *the* key answer to that log-jam problem which is holding us all back. Hence, integration on the basis of equality of voice is indispensible in our essentially tribal subject.

So, where you get the feeling that something you are reading sounds oddball, lateral or off-beam, remember that this is what we are hunting for. Where the analogies are puzzling, please persist, as they are designed to draw you along a logic pathway. Where you become downright embarrassed, enjoy the feeling, as these are the concepts and arguments that you will remember. Where you see some repetition, register it as necessary; these tend to be the points where the tribes and topics of *Extreme Tissue Engineering* truly touch and merge, so they are important for integration.

Here is one last thought to crystallize these points. Some years ago, a prestigious group (Lysaght & Hazelhurst, 2004) prepared a 'state of the nation' review of tissue engineering. This came on the heels of a series of major setbacks in the translation of tissue-engineered products to the clinic and the market. Interestingly, this review paraphrased Winston Churchill's famous speech to conclude that tissue engineering had reached '*the end of the beginning*' (without a question mark).

There is a danger, though, in taking such an optimistic (arguably complacent) position when there are so many other *alternative critiques* of progress in our subject which are possible. We are now several more years further on, and neither the review nor the additional years have substantially changed our tissue engineering paradigm. Given that this paradigm is now more than 20 years old, we might hope to have seen several evolutionary stages or even a couple of minor concept revolutions. Consequently, it is a core assumption of this book that a number of potentially revolutionary concepts *must* be discussed. To return to the Churchillian review; if we cannot *now* identify new strategies, it might be that we are not so much at '*the end of the beginning*' of tissue engineering as '*the beginning of its end*'!

Reference

Lysaght, M. J. & Hazelhurst, A. L. (2004). Tissue Engineering: The End of the Beginning. *Tissue Engineering* **10**, 309–320.

Further reading

Pretor-Pinney, G. (2006). *Cloudspotter's Guide*. Hodder & Stoughton, London. [Beautiful example of sneaking in dry-learning under cover of off-beam entertainment, analogies and stories.]