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### Where do we stand on Organ Printing?

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#### Abstract

Attitude towards organ donation and the risks associated with organ transplantation drive the search for alternatives. One such alternative, albeit a conceptual level, could be the generation of an organ replacement in a controlled setting. For instance, growing suitable cells onto a printed matrix under appropriate conditions would then lead to the formation of a functional organ. How about the practical issues surrounding either duplication or de novo generation of an organ with, say, a device to print a suitable matrix and grow and differentiate cells on it? Here, we wish to outline selected safety-related questions arising from the ex vivo growth, differentiation and maintenance of cells or cell systems.

**Keywords:** Cancer biology, organ printing, transplantation

#### Introduction

Many people associate the term “Trojan” with myths surrounding military tactics. As a backdrop, the city of Troy could not be conquered by the Greeks because of their unshaken stronghold. So, the Greek soldiers decided to infiltrate the fortress by a “Trojan horse”, which carried Greek soldiers. This way, they were able to win this war from within the city of Troy. Aside from the historical context, Trojan Horses are now associated with malware that infiltrates and damages computer systems. These two instances are used to argue in favor of the opinion that the phrase “Trojan entity” is used to describe unfavorable features of a particular object.

Assuring continued patient’s safety and wellbeing are lynchpins of the medical profession. Thus, safety, efficacy and reliability throughout the life cycle of devices for their intended clinical use leaves no room for doubt that features resembling “Trojan entities” are to be assiduously avoided in the development and refinement of implants, to name one out of many examples of devices used in clinical settings.

With citizens benefiting from technological advances by extending quality and duration of life, leaving non-natural causes of demise, such as violence and catastrophic events, aside, the issue of an increased demand for readily available transplantation material cannot be neglected. This, among many others, fuels the attempt of separating transplantation medicine from socio-ethical challenges associated with organ donation.

#### Discussion

One approach to reach this goal might be to use the technology of the 3D-Printer [1,2]. Its technical advance could possibly generate synthetic parts of the body, which could be liked as a matrix to support natural processes (see [3] for further reading on notions pertaining to morphogenetic fields). As for bone matrices, osteoblasts contribute to the synthesis of bone matrix, and the printed biomaterial could be likened as a platform for bone repair.

As for the generation of a matrix for organ transplant, extracellular matrix material, such as collagen, is reported to be used in a clinical setting although the patient who received the cultured skin auto-graft declined follow-up studies, as reported by Zöller et al. [4]. Credence for this notion comes from a series of successful studies where solubilized collagen served as carrier for the skin graft used [5,6].

Published evidence argues persuasively in favor of the notion that cells react to a removal from their natural environment, e.g. the tissue inside the body, to an artificial environment, such as a culture dish with medium inside an incubator oven. Depending on the condition, immortalization and tumorigenic potential may occur.

For illustration, the tumorigenic transformation of a cell is selected, and classical papers are referenced to show selected lines of understanding and implications of the reported studies: Hayflick [7] described a limited number of population doublings of human diploid cells in an ex vivo setting. In agreement with earlier publications [8,9], where the induction of the proto-oncogene c-jun by serum is described, Takahashi et al. [10] report a spontaneous immortalization and malignant transformation of primary, human endothelial cells after prolonged culture in serum- containing growth medium. This immortalization, or, in other words, continuous progression through the cell cycle, appears to involve negative p53 regulation [11]. Note that these observations tie in nicely with the hypothesis that a ‘multiple hits’ lead a healthy cells onto the oncogenic path [12,13].

Some cells go through this crisis without any alteration in their metabolism and/or programming and others do not. Furthermore, the possibility of a malignant transformation by other factors or their influence on the balance of physiological

processes cannot be neglected. Two examples are cited to illustrate the point: Border and Ruoslahti and Minton [14,15], as well as the references therein, illustrate a light and dark side of TGF- $\beta$ , whereas Switzer et al, Larocque et al, and LeBreton et al. [16-18] provide excellent reading regarding current understanding of the biology of primate T-lymphotropic viruses and associated oncogenic events after infection of target cells occurred.

## Conclusion

Would it be possible to create ideal biomaterials that are compatible to our highly complex body? Safety considerations, such as the risk of malignant transformation of cells in, say, an ex vivo culture setting and/or the combination of soluble factors used to supplement growth media cannot be neglected. This question of patient safety must be addressed.

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