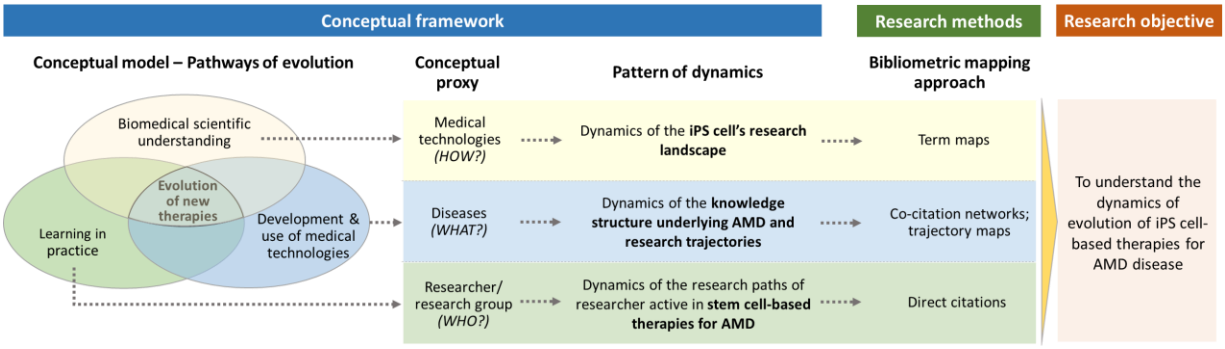
What's behind the curtain? – Dissecting the dynamics of evolution of emerging stem cell-based therapies

Background

The need to diagnose, cure, and treat diseases has existed since the beginning of humanity. Newly emerging technologies have radically altered therapeutic options, such as gene therapy, personalized medicine, and cell therapies (Steltzer et al, 2015). The discovery of induced pluripotent stem cells (iPS cells) in 2006 is expected to revolutionize the use of stem cells for therapeutic purposes. Innovative research with stem cells has long emphasized their potential for market-ready applications, focusing mostly on prescriptive solutions to close the 'translational gaps'. Topics such as scalability, good manufacturing practices, and standardization, are common (Neofytou et al, 2015). However, there is limited understanding of the processes involved in the emergence and progress of iPS cell-based therapies. This manuscript explores these processes by focusing on three aspects (Morlacchi and Nelson, 2011): (i) understanding the diseases, (ii) development and use of medical technologies, and (iii) therapeutic approaches and learning in practice. As depicted in Figure 1, each of these pathways focuses on particular conceptual proxies and dynamic patterns. The case of the eye disease Age-related Macular Degeneration (AMD), the first iPS cell clinical transplantation approach, has been included in this study.

Figure 1: Summary of conceptual framework and research methods



Research Methods

As shown in Figure 1, the dynamics of pathways were determined by diverse bibliometric mapping approaches that were further confirmed by experts. The dynamics of the research landscape on iPS cells were evaluated on the basis of term maps from publications indexed in the Scopus database for the time periods 2006-2008, 2009-2011, and 2012-2014. Co-citation networks were used to characterize the knowledge structure underpinning the research on AMD disease, as inferred from its publications in the Thomson Reuters database for the years 2000-2014. Subsequently, the research trajectories were determined by mapping topics stressed over the years. For both analyses, we used software tools, such as VantagePoint, VOSviewer, and Pajek. Finally, the study of the research paths adopted by iPS cell scientists was conducted using the direct citation analysis approach embedded in the software CitNetExplorer. Five key scientists were selected for this study: Masayo Takahashi (Riken CBD, Japan), Peter Coffey and Robin R. Ali (UCL, UK), David R. Hinton (University of Southern California).

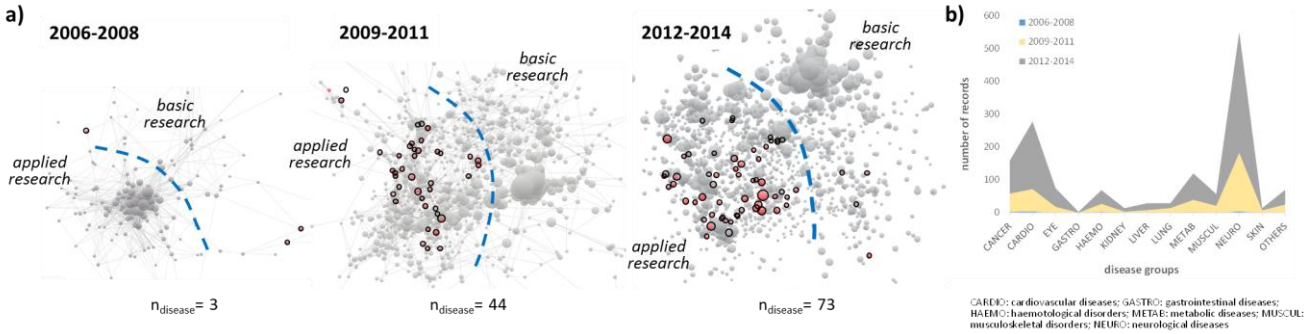
Findings and Discussions

Dynamics of iPS cell's research landscape

The longitudinal study of the term maps demonstrates the increasing attention that research on iPS cells received since the year 2009. These maps depicted a clear demarcation between basic-oriented and

clinical-oriented terms (dotted lines in Figure 2a). The clusters in these term maps revealed knowledge structures classified on the basis of organs and tissues of interest (heart, eye, brain, kidney, etc.). After focusing on terms depicting specific diseases (black-rimmed nodes in Figure 2a), significant differences in the rates of growth across disease groups were observed. As shown in Figure 2b, cancer, cardiovascular, and neurodegenerative diseases had the highest intensities. These differences are due to disease incidence rates, knowledge regarding particular diseases, existence of therapies, etc.

Figure 2: a) Term maps with disease-specific nodes, b) Disease group trajectories



Dynamics of knowledge structure and research trajectories of AMD disease

The knowledge structure underpinning the AMD disease consisted of 49 clusters embracing six general topics: imaging techniques, cost and quality life issues, risks and incidence, genetic risks, drug- and radiation-based therapies, and stem cells and cell transplantation approaches. The longitudinal interactions between these aspects revealed gradual transition from pathogenesis, etiology, and risks associated with AMD disease to the development of imaging techniques and therapeutic approaches, including stem cell transplantation approaches

Dynamics of the research paths of scientists

There was considerable variation in the way the researchers working on the development of stem cell therapies for AMD accumulated knowledge, as confirmed on the basis of the structure of their citation networks. Such differences have led to the development of different transplantation procedures and techniques with respect to the types of stem cells used, methods of transplantation, and transplantation media. Interestingly, these differences have resulted in completely different paradigms for the treatment of retinal degeneration diseases: retinal pigment epithelium- vs. photoreceptor-based cell therapies. However, over the years there has been a converging trend for standard transplantation procedures.

Conclusions

This paper attempted to disentangle what lies behind progress in the emerging field of iPS cell-based therapies for AMD disease by quantitative exploring three pathways of evolution of medical therapies. The global picture of the complexities surrounding cell therapies provided by this paper can contribute to understand this revolutionary field. Current work is focusing on complementing this study with patent data.

References

Morlacchi, P. & Nelson, R.R. (2011). How medical practice evolves: Learning to treat failing hearts with an implantable device. *Research Policy*, 40, 511-525.

Neofytou, Evgenios, et al. "Hurdles to clinical translation of human induced pluripotent stem cells." Journal of Clinical Investigation 125.7 (2015): 2551.

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