



Editorial

An appraisal of the latest achievements on platelet lysate designed for clinical opportunities in regenerative medicine and cellular therapy



In this issue of What's Happening, I have invited my most long-standing friend and colleague, Professor Thierry Burnouf, the Vice-Dean of the College of Biomedical Engineering, Taipei Medical University, Taiwan, as an international team leader on this topic, to concisely share his enormous laboratory and pre-clinical experiences regarding the current status of platelet lysates and their clinical applications with the readers of *Trasci*. Many in *Trasci* are undoubtedly familiar with Thierry' visionary clairvoyance, as team builder and team leader, as in the recent past, we have published a series of manuscripts; international forum; and theme articles on various topics mutual interest including the progression on improving the quality and safety of platelet lysates derived from outdated platelets concentrates and their use in health and diseases.

Currently, numerous studies are carried out on the state-of-the-art use of human platelet lysate for cell therapy, clearly demonstrating that human platelet lysates [HPL] made from outdated platelet concentrates can substitute for fetal bovine serum as xeno-free growth medium supplement of therapeutic expanded human cells for many cell-based therapies. Today, numerous types of mini pools of HPL are produced either in blood establishments or by biopharmaceutical companies, often requiring the implementation of pathogen inactivation procedures, with the removal of residual leucocytes from platelet concentrates, to improve the safety of such bioproducts in advanced cell therapy. Residual leukocytes in platelet concentrates may substantially affect the intrinsic biology and properties of platelet-derived products by enhancing the wound healing process, immune function, and antibacterial potential. Hence, a better understanding of the potential impact of leukocytes in platelet concentrates used to produce HPL probably requires some meticulous quality monitoring and in-depth risk mitigation assessments. This approach would be in line with the current regulatory requirement for any clinical applications in human cell propagation or direct clinical applications in some broader frontiers such as in oral-maxillofacial surgery, periodontal surgery, plastic surgery, orthopedic surgery, and sports medicine, and other clinical interventions based on delivery of multiple trophic factors, offering a highly promising approach for optimising haemostatic and wound healing management. Moreover, thanks to its richness, HPL opened up some newer frontiers in advanced cell therapy where the platelet secretome provides huge amounts of growth factors, antioxidants and anti-inflammatory proteins, cytokines, and chemokines, and other crucial biological entities, such as extracellular vesicles, required in healing processes and to treat different diseases such as recalcitrant ulcers, alopecia, oral mucositis, radicular pain, osteoarthritis, and cartilage and tendon disorders to name a few. In addition, the abundant presence of growth factors and chemokines

stored in platelet granules that are naturally released by different strategies, mostly through freeze/thaw, lyophilization, sonication, or thrombin activation, make HPL a potentially powerful biotherapy for clinical orthobiologic applications or for the treatment of musculoskeletal injuries, apart from some of its applications in regenerative and advance cell therapy for targeted personalised medicine. In fact, recently an extrusion-based bionics platelet lysate with a highly promising future was developed that equally meets all essential requirements of rheological, mechanical, and stiffness properties of native skin tissue and with high degrees of cellular viability, cell attachment and growth factors, and deposition by dermal fibroblasts after two weeks of culture.

In the following manuscript, Thierry provides a personal viewpoint commentary on some specific items including recent investigations carried out in his laboratory entitled: "Regenerative lives of expired platelet concentrates in human biotherapy; an update", raising the bar in the use of a promising safer platelet lysate biotherapy by integrating multidisciplinary laboratory experiments and animal models, demonstrating that:

- i In mouse models of Parkinson's disease, the intranasal administration of a specially engineered platelet lysate does not induce side effects, diffuses into the brain, and provides a neuroprotective effect of dopaminergic neurons;
- ii In mouse models of traumatic brain injury, the topical brain application and intranasal delivery of this platelet lysate consistently improved motor function and reduced inflammation, reactive oxygen species levels, and the loss of cortical synaptic proteins;
- iii By using the unbiased proteomic analyses his team confirmed that HPPL reversed several transport pathways, post-synaptic density, mitochondria, or lipid metabolism and strongly supports, for the first time, that human platelet lysate is a strategically reliable and effective therapeutic source of neurorestorative factors that deserve urgent in-depth consideration for universal brain trauma treatment;

Finally, concluding that developing highly standardised and dedicated virally safe and efficient human platelet lysates for ex vivo expansion and applications in specialised advanced cell therapy and regenerative medicine, still remains undeniably one of the major areas of research and development goals as we are witnessing from the current treatment outcomes and the journey in this direction already begun and limitless and so far are far from ideal.

I wish to take this opportunity to express my sincere thanks, to Thierry for accepting my invitation and submitting his timely viewpoints, which are of high educational value to the benefit of all readers.

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Clearly, we have not yet seen the end of outdated HPL therapy. I fully recommend the attached original viewpoint commentary, to all readers at this end of the year What's Happening Section of TRASCI.

This highlights again the saying that:

Everything that does not exist can possibly and probably happen in real time and place on a significant basis of reality, the imagination spins, weaving new patterns; a mixture of memories, experiences,

free fancies, incongruities and improvisations. August Strindberg, "A dream play"

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