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Editorial

Past and future of stem cells: from Prometheus to regenerative medicine

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Proceedings

Proceedings of the 2nd International Course on Perinatal Pathology
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Cagliari (Italy) · October 31st, 2015
Stem cells: present and future
Guest Editors: Gavino Faa (Cagliari, Italy), Vassilios Fanos (Cagliari, Italy), Antonio Giordano (Philadelphia, USA)

"Then indeed the winged hound of Zeus, the ravening eagle, coming an unbidden banqueter the whole day long, with savage appetite shall tear your body piecemeal into great rents and feast his fill upon your liver until it is black with gnawing."
Aeschylus, *Prometheus Bound* (ca. 460 BC)

Keywords

Stem cells, regenerative medicine, brain, heart, lung, kidney, adrenal glands, liver, pancreas, gut, milk.

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The salamander limb regenerates completely after amputation and the heart of the zebrafish returns to normal even after an extensive injury [1].

What is it that makes all this possible? The answer is the presence of stem cells, which in these animals are quite efficient. We humans have lost this capacity, but researchers are working incessantly to control cell reprogramming and make regenerative medicine possible and close at hand [1, 2].

Facultative liver stem cells have long been thought to be an important source of new hepatocytes during chronic liver injury. However, even this longstanding paradigm is being challenged by some recent data: contrary to prevailing stem-cell-based models of regeneration, virtually all new hepatocytes come from preexisting hepatocytes [3, 4]. Life is complicated.

All Quiet on the Western Front. It is probable that the ancient Greeks knew about the regenerative properties of the liver. Suffice it to recall the story of Prometheus punished by the gods for revealing the secret of fire. He was chained to a rock where by day an eagle fed on his liver, which regenerated itself punctually during the night (**Fig. 1**) [5].

The Proceedings of the 2nd International Course on Perinatal Pathology (part of the 11th Inter-

Figure 1. Vector illustration inspired by a Laconic Kylix representing Atlas and Prometheus (560-550 BC, found at Cerveteri and now at Vatican Museums, Rome). Prometheus is chained to a rock. During the day an eagle feeds on his liver, which regenerates during the night.

national Workshop on Neonatology), held in Cagliari (Italy) on October 31, 2015, are presented in this issue and in the previous issue of the *Journal of Pediatric and Neonatal Individualized Medicine*. These papers, the fruit of the work of many researchers, fit into this ancient and at the same time most modern scenario. The hard core of researchers in the Division of Pathology and the Neonatal Intensive Care Unit, Neonatal Pathology and Nursery of Cagliari is supported by a group of international collaborators from the United States, Germany and Belgium, thus ensuring a significant interdisciplinary approach. And so, the itinerary, or better still the adventure, must necessarily start from the brain, the noblest organ, the most complex "thing" in nature.

The first two articles analyse the different refined pathways used by neural stem cells in the diverse stages of their proliferation and differentiation [6, 7]. These studies may be fecund in many areas, but undoubtedly one of the most fascinating is represented by the possible practical consequence in the preterm neonate's brain for the prevention and treatment of cerebral degeneration in the adult [8].

And what about the heart? An open future or a mirage? This is the question posed by one [9] of the two articles [10] devoted to this organ. If we observe experiments on animals, we find reasons for optimism [11]. Neonatal immunohistochemistry can shed light on intriguing correlations between perinatal markers, aging, and carcinogenesis.

The lung is considered a possibly renewable organ considering its ability to respond quickly to cell damage thanks to the presence of multipotent stem cells [12, 13]. These cells represent interesting prospects in the treatment of bronchopulmonary dysplasia [14].

As many as four articles are devoted to the adrenal gland [15] and kidney [16-18], with an eye on kidney physiological regenerative medicine in the preterm neonate in preventing chronic renal insufficiency. In the last few years striking progress has been made in understanding cell connections at the interface between stem and progenitor cells in stem-cell niches [16]. We have extensively studied this topic and the potentialities of renal regeneration [19-26].

In spite of the intuitions of the ancient Greeks, much work needs to be done on the liver. The paper on this organ represents a starting point leading to further contributions allowing more precise characterization of hepatic stem cells [27].

As concerns the pancreas, its stem cells suggest opportunities for transforming the fruits of basic research into clinical tools [28-30].

The gut is considered the second brain and represents a scenario of extraordinary interest owing to the network of bidirectional biological messages exchanged by brain, gut, microbiota, immune system, and stem cells [31-33]. An understanding of the cryptic language of these messages can help us to comprehend and prevent disastrous diseases such as neonatal necrotizing enterocolitis [34].

Last but not least, we must consider the stem cells of mother's milk [35-37] which, from the neonatal intestinal lumen, are transported to the several organs, among which the brain, in which they become neurons, oligodendrocytes and astrocytes. This is a discovery that changes many things with respect to our knowledge today [38].

As can be seen, many actors are present on the stage in the archipelago of complexity and the uninterrupted string of perinatal programming which, from fetus to adult, orients and governs our health, for better or for worse.

We hope that our working together will advance, albeit slightly, our knowledge and understanding, and lead us on towards the future with the enthusiasm and determination of our young colleagues.

We hope that all this research, only in appearance detached from reality, will soon become opportunities for treating all our patients, young or old, who have an extraordinary need for them.

May this science bordering on the imaginary soon become a concrete reality full of hope!

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Vector illustration in **Fig. 1** is by Eleonora Fanos.

Declaration of interest

The Authors declare that there is no conflict of interest.

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