

# Waiting for the spectacle: A stem cell's report

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All of us developed during embryogenesis. Some of us came from oral epithelium; others, from ectomesenchyme (neural-origin tissue). Some were chosen during the intrauterine period of the human being where I used to inhabit, and have received the necessary stimulus to participate in the classical spectacle named "The dental formation". While differentiating themselves into beautiful ameloblasts, odontoblasts, cementoblasts or osteoblasts, each one of them played a specific role and continues to do so.<sup>1</sup>

For a long time I wondered if my job would be restricted to replace the main cells of the show when they could no longer live, as many of my cousins have done. However, in the year of 1976, Friedenstein et al<sup>2</sup> discovered that one of our tribes, the BMMSCs (Bone Marrow Mesenchymal Stem Cells) were multipotent and could differentiate themselves into osteogenic, chondrogenic, adipogenic, myogenic and neurogenic cells. What a glorious moment! Since then, I believed that soon my tribe would

also be discovered, and so it came true: in 2000, Gronthos et al<sup>3</sup> introduced the DPSCs (Dental pulp stem cells); in 2003, Miura<sup>4</sup> et al characterized the SHEDs (stem cells from human exfoliated deciduous teeth); in 2004, Seo et al<sup>5</sup> isolated the PDLSCs (Periodontal Ligament Stem Cells); and finally, in 2006, Sonoyama et al<sup>6</sup> nominated my tribe, the SCAPs (Stem Cells From Apical Papilla) to be part of the most exciting spectacle at all times: "Pulp regeneration state of art".

When I was included into the well-known tissue engineering study group, researchers used to test tribes from the dental region and compare them to the BMMSCs tribe in order to verify our quality standard. To make sure that we were really multipotent cells, our epitopes were labeled with immunoreactive agents and analyzed by flow cytometry. Thus, researchers discovered that we (the SCAPs) express CD73, CD90, CD105 and STRO-1, just like the BMMSCs.<sup>7</sup> Furthermore, we express markers for

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vascular, neurogenic, odontogenic, adipogenic and osteogenic differentiation as much as our cousins, the SHEDs and DPSCs. In the case of PDLSCs, there are no odontogenic markers, but cementogenic ones.<sup>8</sup>

I shall tell you a secret: We are much more effective in forming odontoblastic cells than the famous BMSCs. Curiously, although SHEDs and BMSCs have fast proliferation capacity, they do not have the ability to generate complete pulp-dentin tissue as we (SCAPs) and the DPSCs do. Well, my mother warned me that those in a hurry cannot do anything right. But it is also true that in the presence of neural cell markers, even without differentiation stimulus, the SHEDs already express  $\beta$ -III tubulin, GAD and Neu N. And that is their merit.<sup>9</sup>

I also express lots of these neurogenic markers, but only after induction. I learned about it because Huang et al<sup>7</sup> isolated my sisters from human beings and made them grow in laboratory, using culture medium with neurogenic-inductor factor. The researchers analyzed my sisters' phenotypes with special dyes and fluorescent microscope. My sisters sent me a photomicrograph. How shiny they were!

As I have already mentioned, I was invited to join the "pulp regeneration" spectacle and, nowadays, there has been some negotiation over creating a tooth just like those shaped during embryogenesis. And this means real mineralization, vascularization and innervation. Nevertheless, the aim of developing an entire tooth with enamel in the crown and the root having interactions with periodontal ligament and alveolar bone, unfortunately, has not been achieved so far. Furthermore, there is no evidence of how the signaling process works towards the growth of a normal sized tooth and how its complete eruption functions.<sup>9</sup>

However, there is one matter I am sure about: Yes, we can create parts of a tooth by linking some of my peculiarities with those of my PDLSCs cousins.<sup>7</sup> Perhaps that is the reason why researchers are so anxious to find an ideal scaffold: The three-dimensional structure that lets us feel free to replicate, allows our nutritional exchanges, gives us a direction to grow and still participates in the spectacle. Worst case scenario, it should at least not disturb us. I have been told about the dentin scaffolds previously treated with EDTA; the fibrin scaffolds with platelet-rich plasma<sup>10</sup>; scaffolds with hydroxyapatite and phosphate tricalcium powder;<sup>11</sup> organic scaffolds containing collagenase;<sup>12</sup> and biomaterial made of PLGA or PGA.<sup>7</sup>

Now, let's face it, every famous star has its requirements. My microenvironment must be perfectly adjusted to allow "social interaction" by means of molecular signaling which I need so badly. After giving the matter some thought, I came to the conclusion that growth factors are useful supporters for dental tissue engineering. The VEGF (vascular endothelial growth factor), for instance, is of paramount importance to generate vascular network in such an inhospitable place as the inside of a rigid and isolated tooth. In addition, the release of TGF- $\beta$  (Transforming growth factor- $\beta$ ) by dental tissues also seems desirable for our proliferation and differentiation into odontoblasts.<sup>12</sup>

Lastly, my artistic name will be "*odontoblast-like cell*". However, while my stardom does not rise, I remain here at the laboratory studying the chapter about "Pulp regeneration" which will be soon disclosed. Anyhow, we are getting ready so that, in a near future, we will appear in the best theaters across the world, leaving behind "The Implant Musical" which has already occupied its space.

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