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Re: Characterization of the Early Proliferative Response of the Rodent Bladder to Subtotal Cystectomy: A Unique Model of Mammalian Organ Regeneration

CC Peyton, D Burmeister, B Petersen, KE Andersson, and G Christ

Expert's summary:

In a recent study [1], adult female rats were subjected to subtotal cystectomy (STC; removal of 75% of the bladder), and at 1, 3, 5 and 7 days, injected intraperitoneally with bromodeoxyuridine (BrdU) 2 hours before their bladders were harvested for histological examination. In control bladders, less than 1% of cells were labeled with BrdU, but in STC bladders between 5 and 8% were labeled. In regard to the distribution of BrdU+ cells in STC bladders, ~65% were in the epithelium (EP) at 1-day, ~80% in the lamina propria (LP) and muscularis propria (MP) at 3 and 5 days, and then equally in the three compartments at 7-day. Co-staining for BrdU with cytokeratin, vimentin or smooth muscle actin (SMA) identified the contribution of epithelial, interstitial, and smooth muscle cells to the STC-induced proliferative activities. However, most BrdU+ cells were devoid of these cellular markers and thus are possibly progenitor cells. STC also caused an increase in staining for sonic hedgehog (Shh) and its downstream effectors Gli-1 and BMP-4, suggesting the involvement of the Shh pathway in bladder regeneration. The authors concluded that STC bladder is an excellent model for studying the molecular and cellular mechanisms of organ regeneration.

Expert's opinion:

This is an excellent study that extends the author's previous study, in which rat bladder was shown to fully regenerate in 8 weeks after STC [2]. While the earlier study focused on the functional characterization of the fully regenerated bladder, the present study investigated the early-stage cellular response of bladder regeneration. To examine cellular proliferation, immunofluorescence was performed for BrdU detection, and to reveal the cellular identity of BrdU+ cells, co-staining was performed for cytokeratin, vimentin, and SMA. The resulting histological images are of excellent quality and expertly interpreted. However, for studying the Shh pathway, the staining method was switched to immunohistochemistry (IHC) without explanation, and the resulting data are not as convincing. More importantly, since IHC does not permit co-staining for BrdU and cell markers, whether there was an association between Shh-pathway and proliferating cells could not be established. In any event, the "global" proliferative response in the STC bladder is reminiscent of the random distribution of EdU+ cells in the developing rat bladder [3] (EdU is similar to BrdU). In other words, the regenerating or developing bladder cells do not fit the expectation of being "bladder stem cells". Rather, they appear to originate from an outside source - perhaps the bone marrow.

Authors:

Dr. Ching-Shwun Lin, Department of Urology, University of California, San Francisco, CA 94143-0738, USA, Phone: 415-476-3800, Fax: 415-476-3803, clin@urology.ucsf.edu

Dr. Tom F. Lue, Department of Urology, University of California, San Francisco, CA 94143-0738, USA, Phone: 415-476-1611, Fax: 415-476-8849, tlue@urology.ucsf.edu

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