Back to the future but better

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Vascular interventions cause arterial injury and induce a complicated and temporal response to injury that, under ideal conditions, leads to healing, but under pathologic conditions leads to a persistently deranged vessel. The rat model of balloon angioplasty injury has been well-described and is useful to our understanding of the vascular response to injury.

In a series of seminal manuscripts, Alec Clowes demonstrated the power of the rat carotid artery injury model on revealing fundamental mechanisms and time points (proliferation [2 days], migration [7 days], proliferation [14 days], extracellular matrix [>14 days]) by which vascular smooth muscle cells participate in pathologic vascular remodeling that continue to pester clinicians and vascular patients on a daily basis.[1-7]

In this article, Samuel Röhl et al[8] present a comprehensive exploration of the temporal molecular response to the carotid balloon angioplasty model in rats. This 20-author and multinational report brings together a diverse international group of investigators, using cutting edge methodologies that were not available in the past, to discover the molecular signaling pathways that are most abundant in this model.

Methodologically, the authors performed balloon angioplasty on the carotid artery of 69 male rats that were then humanely killed at the following time points: 2 hours, 20 hours, 2 days, 5 days, and 2, 6, 12 weeks.

Exciting discoveries include the upregulation of immune cells and pathways (in addition to the well-known impact of platelets also validated here) in the early response phase. The authors found that it was lymphocytes early (<2 days) and macrophage later (out to 5 days). The role of immune cells in pathologic arterial remodeling, although recognized for years, is only now getting the attention deserved. This publication will certainly be useful in stimulating discovery science on this topic. The authors also demonstrate a number of relevant pathways to arterial remodel that seem to flip flop in a predictable pattern in this model as demonstrated in Figs 2 and 4. Of note, the authors found that these animals were able to demonstrate a return to contractile features in vascular smooth muscle cells at late time points, supporting a role for this model in healing profiles. Finally, the authors provide an open source dataset with these longitudinal profiles that may be of use to investigators as we strive to validate clinically relevant pathways in patients and then develop novel therapeutics that can help our patients to better approximate the healing seen in healthy male rats.

I thoroughly enjoyed this manuscript, and I am grateful to the authors for publishing in our Journal.

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