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Angina.com Interview with: Clint S. Robbins, PhD

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Angina.com: What are the main findings of the study?

Answer: Our study redefines how inflammation arises in atherosclerotic disease. The previous assumption was that plaque macrophages, a key cell type that drives atherogenesis, derive mainly from the recruitment of their precursors, monocytes, from the circulation. Our study demonstrates that macrophages can proliferate locally within the plaque itself. In other words, macrophage self-renewal is a major component of atherosclerosis.

Angina.com: Were any of the findings unexpected?

Answer: Our findings were unexpected. We anticipated cell recruitment to play a much larger role. Our studies revealed that while early atherosclerosis depends on monocyte influx, as disease progresses, macrophage accumulation becomes increasingly more dependent on macrophage proliferation.

Angina.com: What should clinicians and patients take away from this study?

Answer: There is considerable focus by the research community to test the benefits of blocking leukocyte recruitment. Moreover, pharmaceutical companies are thinking about bringing these approaches to humans. According to our observations, caution is required, and alternative (additional) approaches should be explored. Blocking recruitment may not be efficacious if lesional macrophages sustain themselves through cell division. Is blocking monocyte influx a sound therapeutic strategy or should we be focusing on macrophage proliferation, or both, depending on context?

Angina.com: What further research do you recommend as a result of your study?

Answer: We are currently pursuing several questions. Do all macrophages proliferate or

only specific subsets? Determining which cells divide will be important for identifying therapeutic targets. Is proliferation a general feature of atherosclerosis, or is it important at only specific stages of disease? What are the underlying mechanisms that drive macrophage proliferation in atherosclerosis? Finally, do our findings translate to human disease? Work by our group and others have demonstrated that macrophage proliferation also occurs in human atherosclerotic plaques. The current challenge is to determine its relative importance to disease progression.

Citation:

Local proliferation dominates lesional macrophage accumulation in atherosclerosis

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