



Introduction	Method	Result	Conclusion	Future Direction
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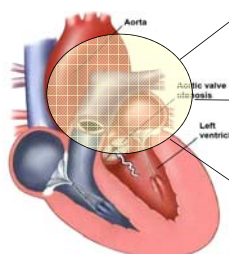
An Animal Model for Aortic Calcification

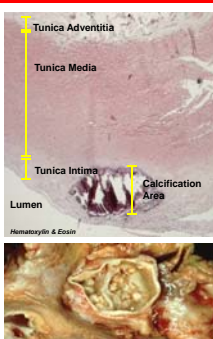
By: Dr. Zuhier Awan, MD, MSc, PhD, DABCL, FACB, FRCPC, FAHA, FACE




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Aortic Valve and Wall

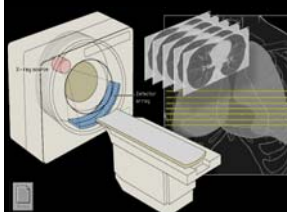








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CT Scan of Aorta





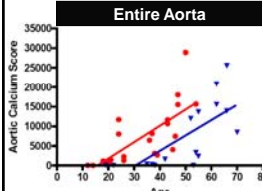
Awan et al, ATVB. 2008 Apr;28(4):777-85.



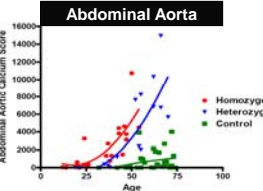
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Follow-up of 22 Heterozygous FH


Entire Aorta



Abdominal Aorta



Alrasadi et al, Am Heart J. 2009 Jan;157(1):170-6.



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Bone Marks DEXA Scan

Calcium homeostasis and skeletal integrity in individuals with familial hypercholesterolemia and aortic calcification.

Awan Z, Alwaili K, Alshahrani A, Langsetmo L, Goltzman D, Genest J.

Cardiovascular Research Laboratories, McGill University Health Centre and McGill University, Montreal, Quebec, Canada.

Awan et al; Clin Chem. 2010 Oct;56(10):1599-607.



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Hypothesis

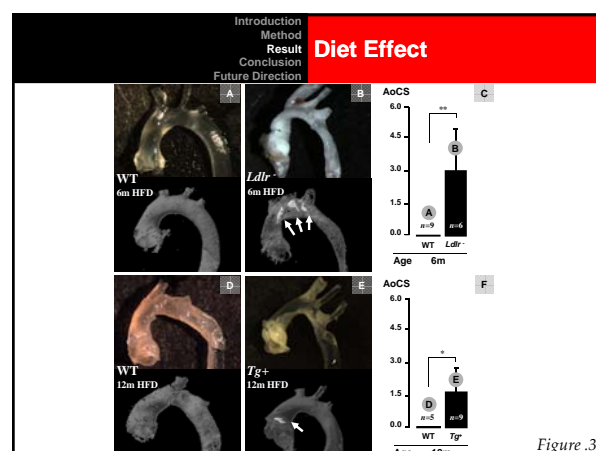
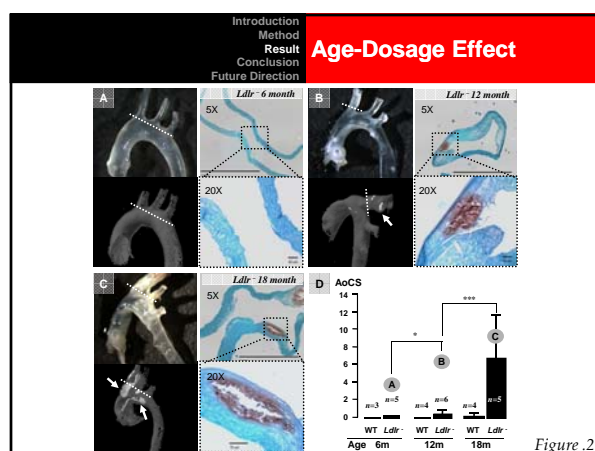
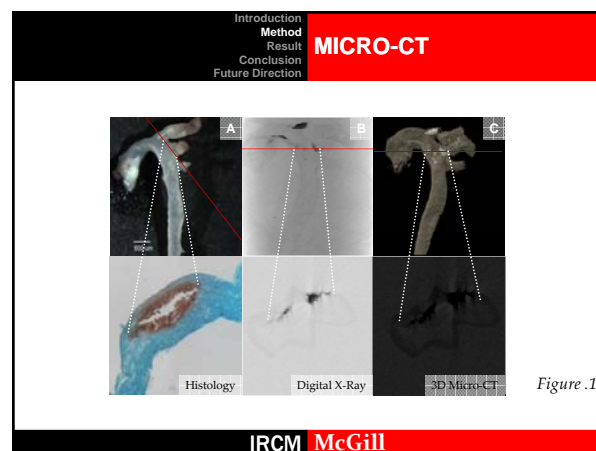
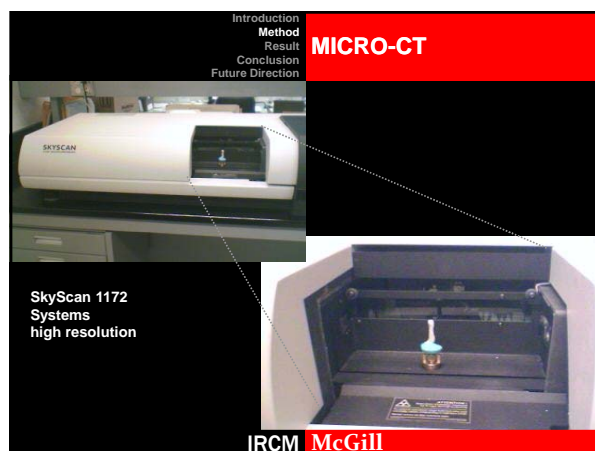
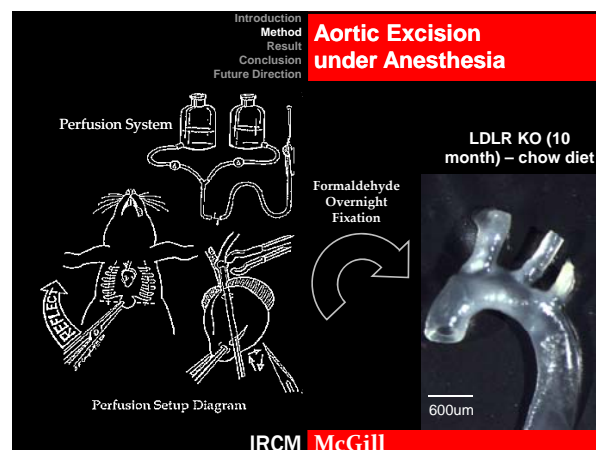
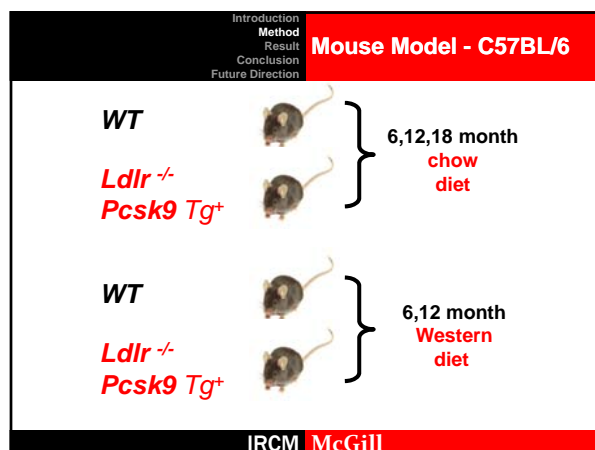
Hypothesis:

- The degree of LDLR-deficiency is related to the extent of calcium deposition at sites of vascular injury and does not correlate with circulating cholesterol levels.

Plan:

- Develop a model for aortic calcifications.
- Study aortic calcification in *Ldlr*^{-/-} and *Pcsk9*^{GOF} mice using a sensitive method.





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<h2>Relationship with Cholesterol</h2> <p>We compared WT on HFD to LDLR KO on chow diet:</p> <ol style="list-style-type: none"> 1) Extensive calcifications were observed in LDLR KO chow-fed mice 2) Despite similar cholesterol levels in WT mice fed a HFD, no detectable calcification was observed. 				

Calcification is independent of cholesterol level

Figure 4

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<h2>Relationship with Cholesterol</h2> <p>We compared <i>Pcsk9</i>^{GOF} to LDLR KO both on chow diet at age 18m:</p> <ol style="list-style-type: none"> 1) Extensive calcifications were observed in LDLR KO on chow diet. 2) Magnitude of cholesterol and calcification was in between WT and LDLR KO. 				

Gene-dosage effect on Calcification in *Pcsk9* Tg+

Figure 5

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<h2>Summary</h2> <ul style="list-style-type: none"> ▪ We developed an animal model for aortic calcification and validated this with a sensitive method. ▪ We established that the LDLR-deficient status is a triggering factor for osteoblast differentiation. ▪ <i>Pcsk9</i>^{GOF} confirm the possible role of LDLR in the extent of calcium deposition. 				

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<h2>Proposed Experiment</h2> <p>Testing single and/or combination therapies:</p> <ul style="list-style-type: none"> ▪ Chelation and Demineralization Therapy. ▪ Vitamin K. ▪ Statins. ▪ Estrogen. ▪ Selective estrogen receptor modulators (SERMs). ▪ Calcium Channel Blockers (CCBs). 				

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<h2>Questions</h2> <div style="text-align: center;"> <p>Thank You</p> </div>				

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