Regulation of miRNAs in cardiovascular medicine: potential impact on platelet function and future perspectives

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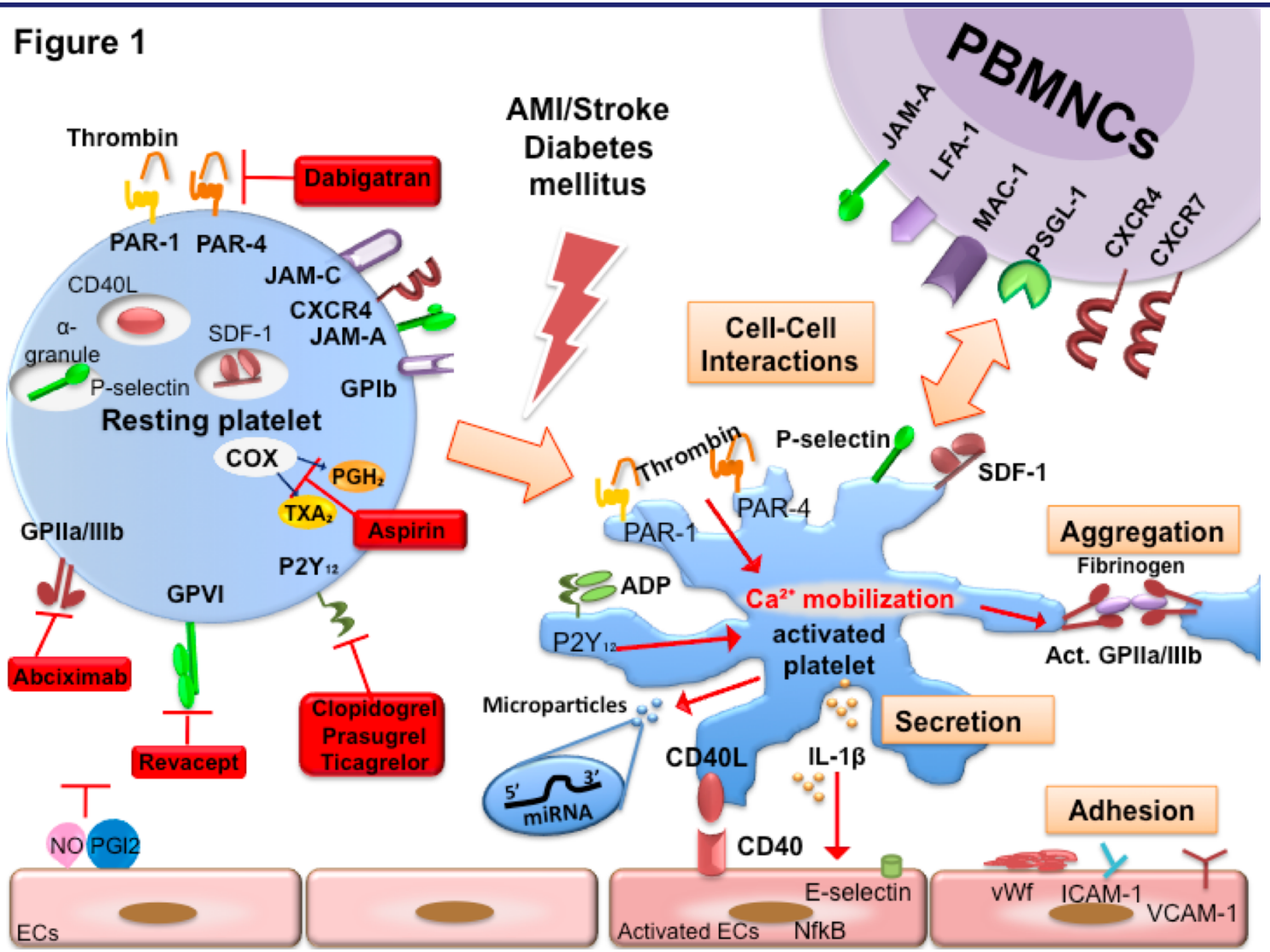
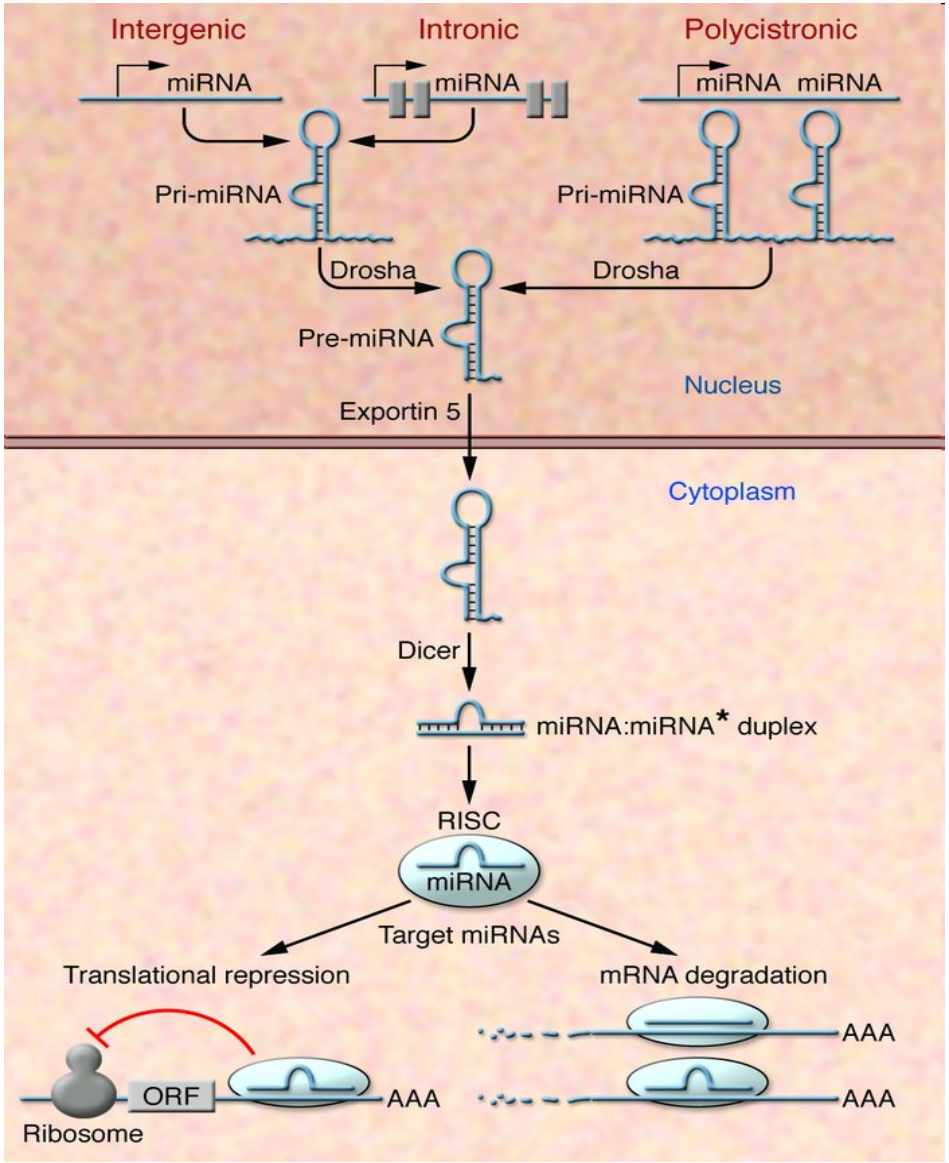
Platelets in Vascular Homeostasis



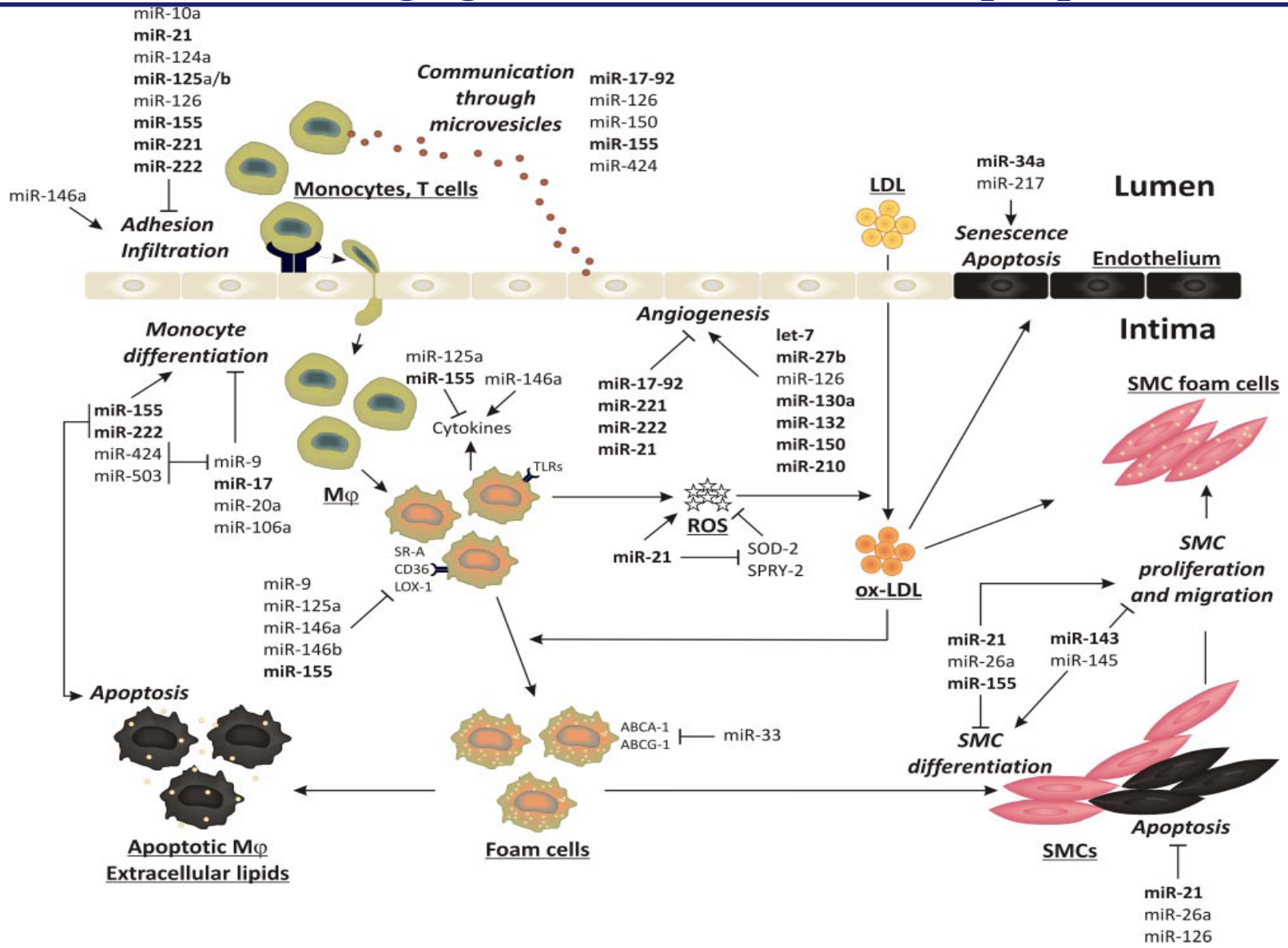
Stellos K, Curr Vasc Pharmacol, 2012 In Press

miRNAs: powerful new regulators of vascular biology and provocative therapeutic targets



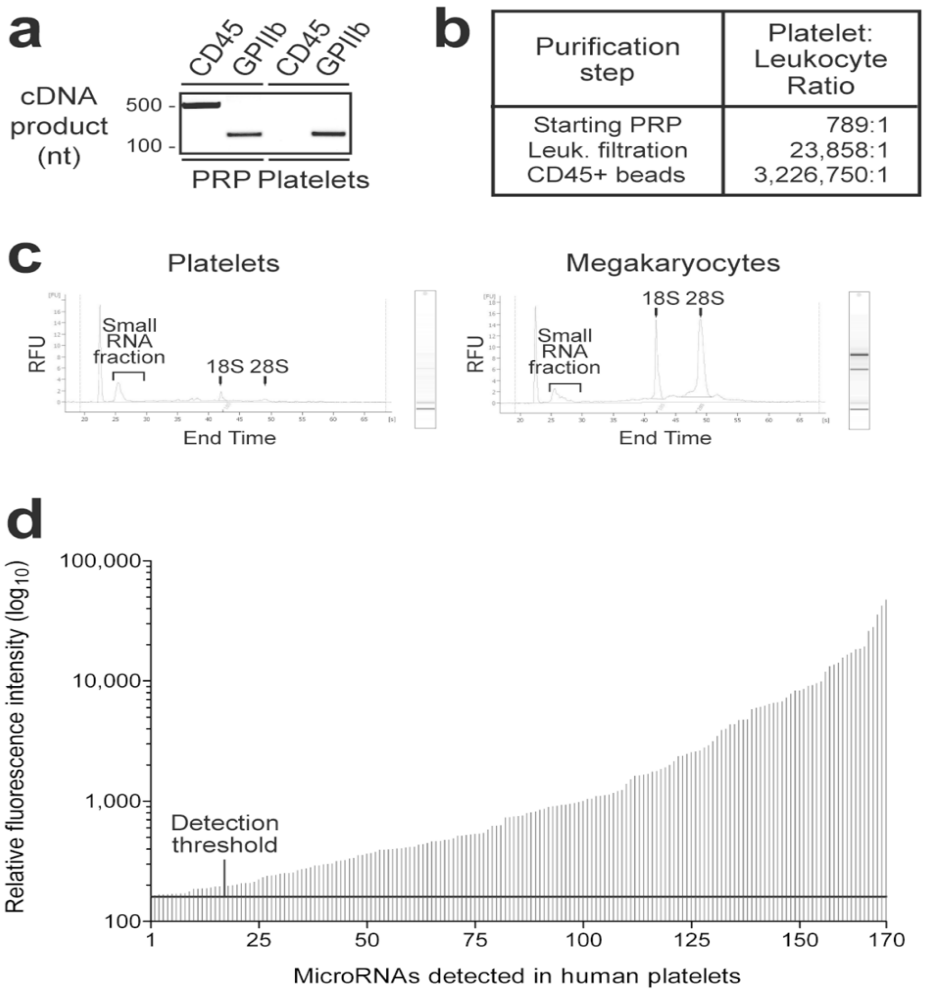
Van Rooij, J Clin Invest, 2007

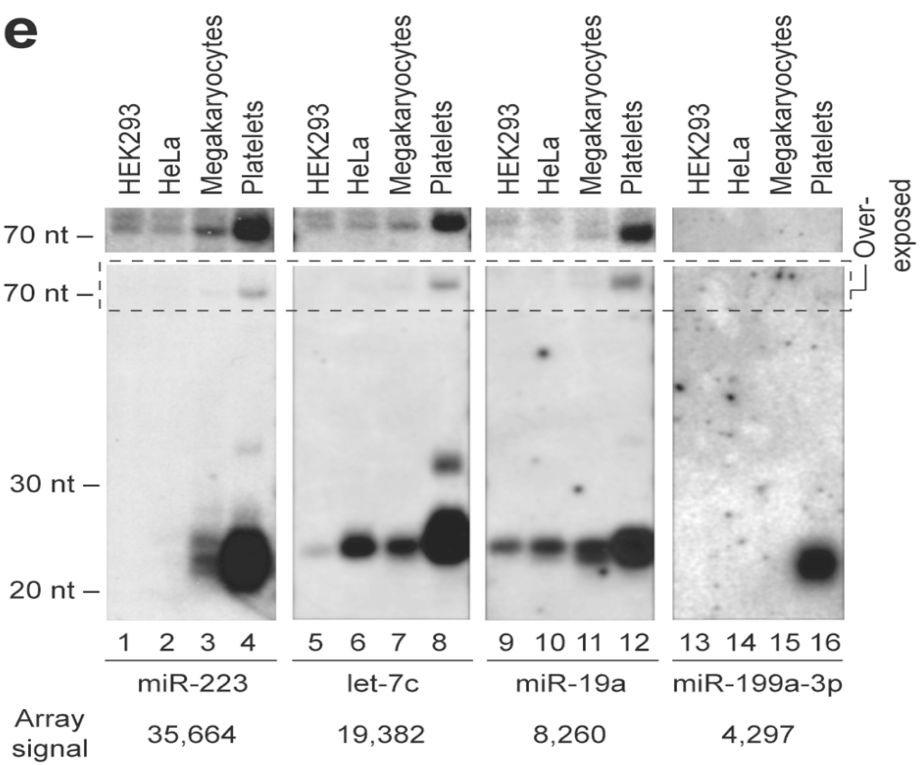
miRNAs regulate inflammation, oxidative stress, apoptosis, and angiogenesis in atherosclerotic plaques



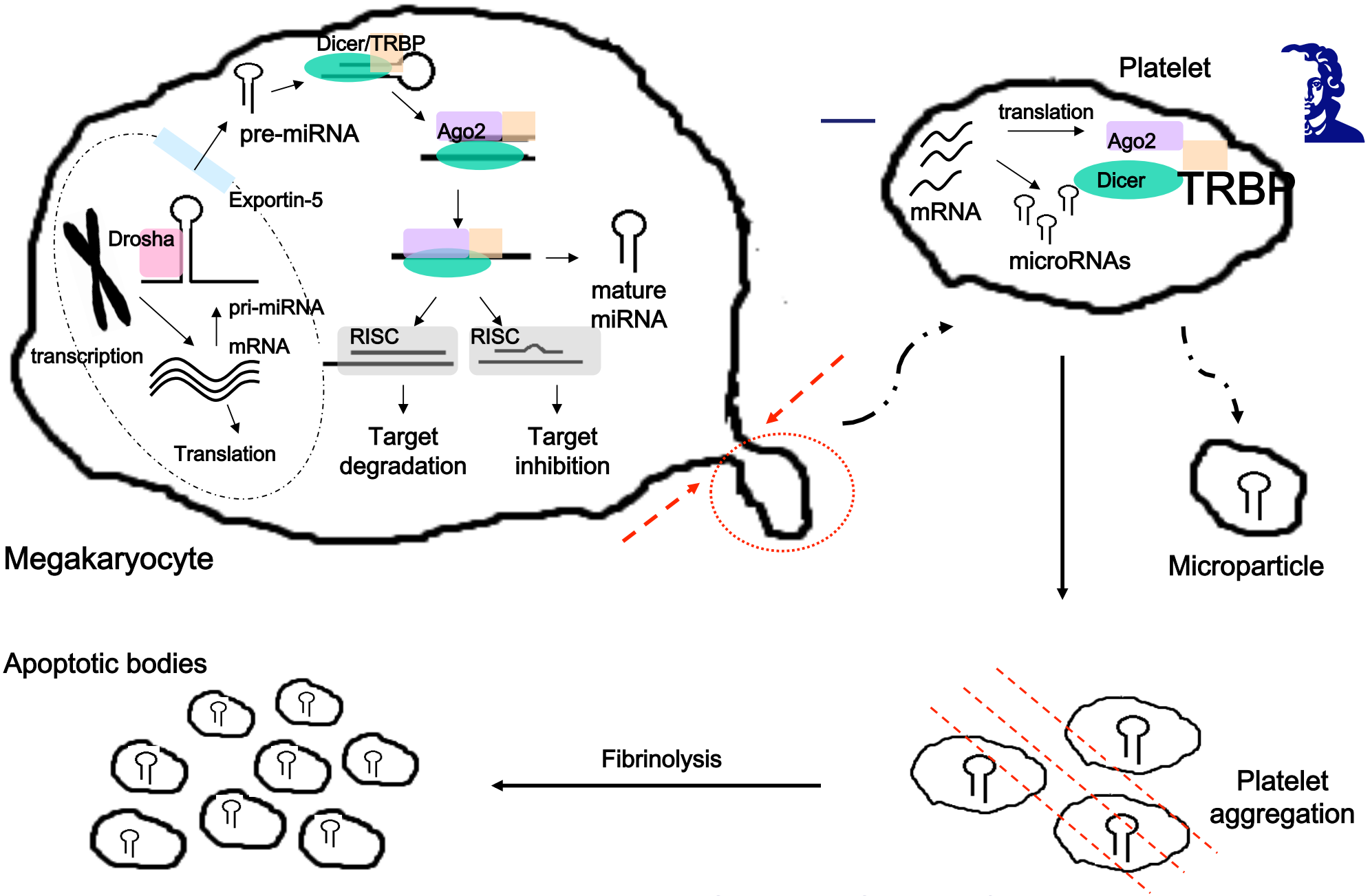
Hulsmans M,
Faseb J, 2011

Human platelets contain an abundant array of miRNAs



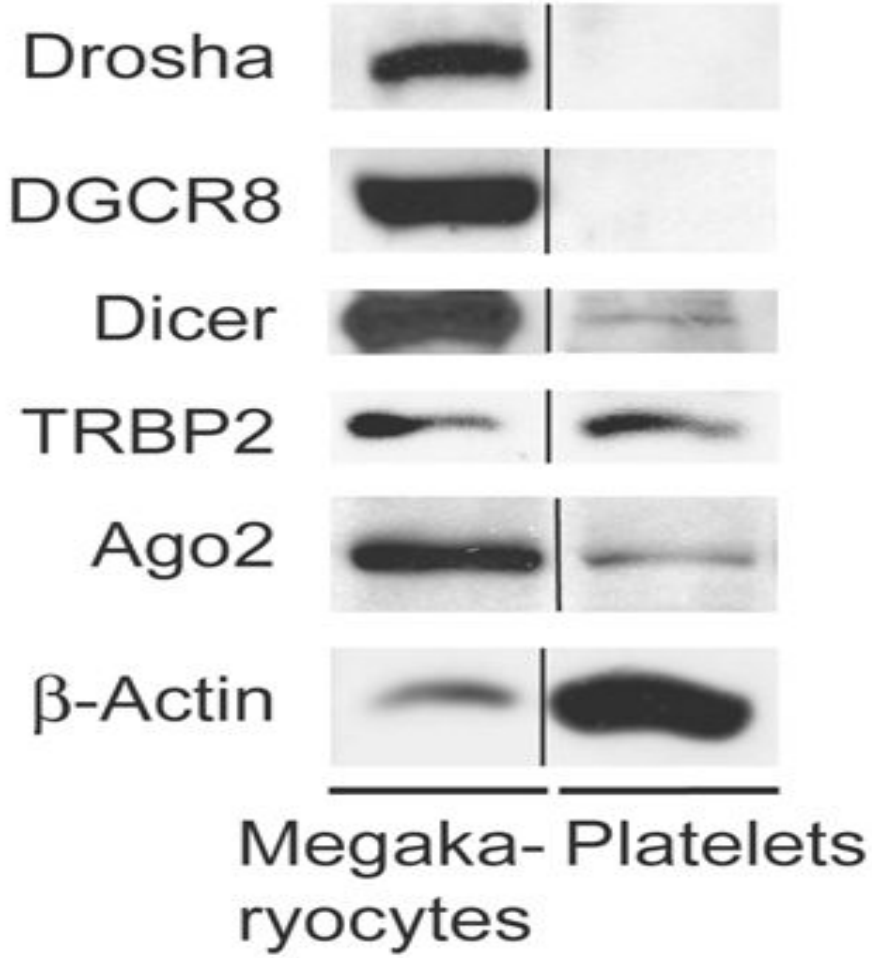


Landry P, Nat Struct Mol Biol, 2009



Gatsiou A…Stellos K, Curr Vasc Pharmacol, 2012

MiRNA biogenesis machinery exists in platelets

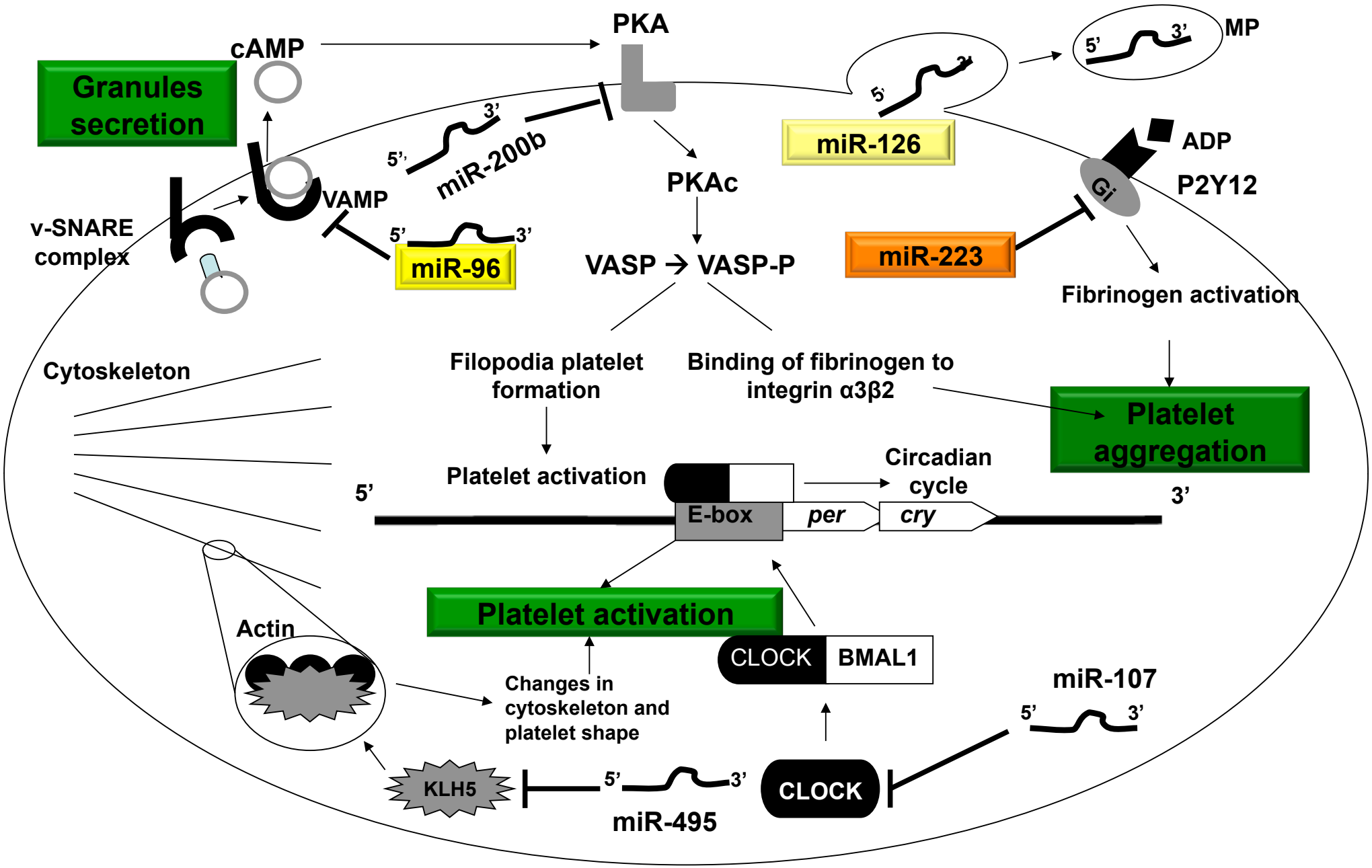


Landry P, Nat Struct Mol Biol, 2009

Role of miRNAs in megakaryocytopoiesis

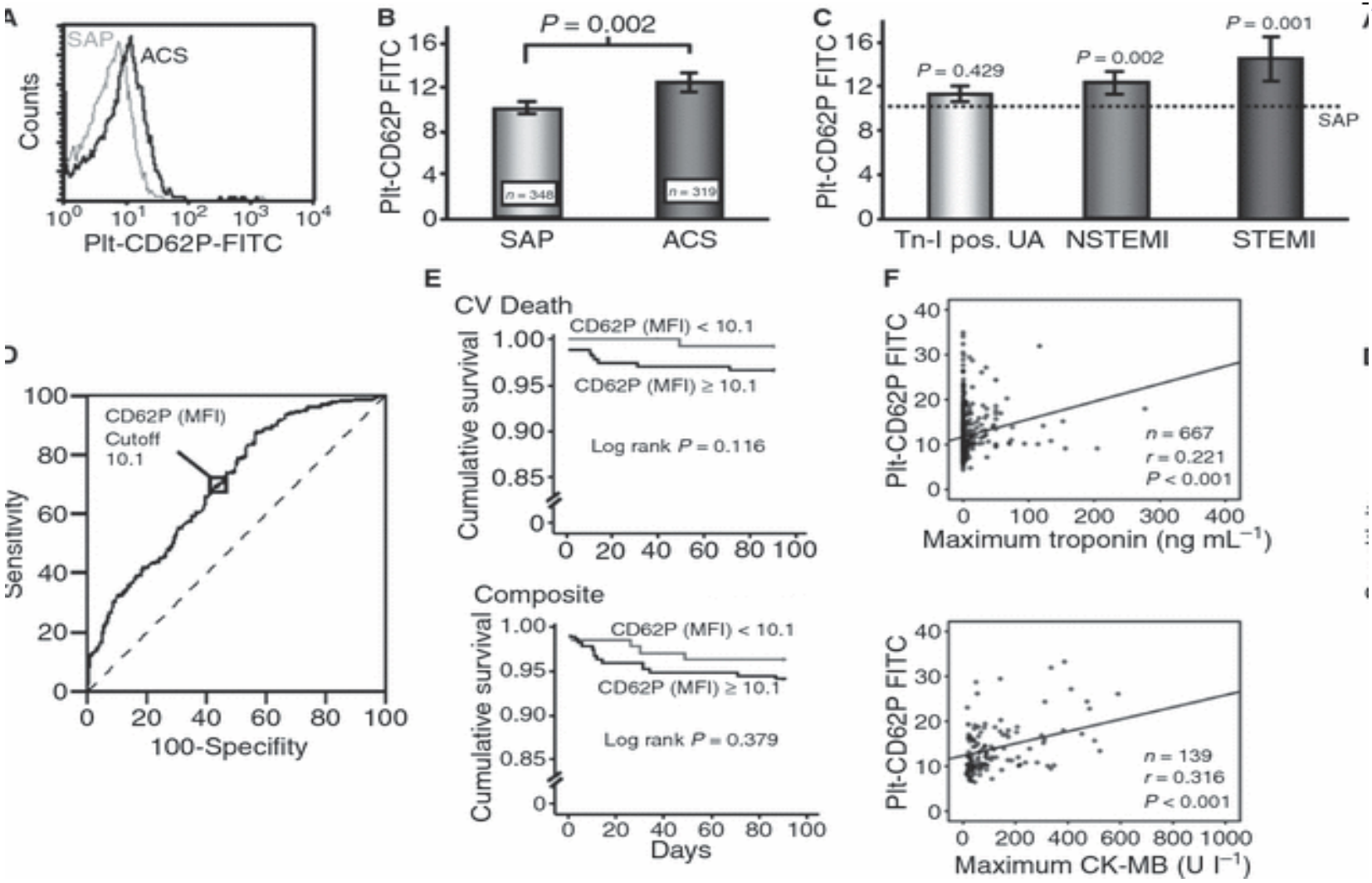
miRNAs	Role in megakaryocytopoiesis	References
miR-10a,-126,-106,-10b, -17,-20	Downregulated in megakaryocytopoiesis and may unblock involved target genes	[12]
miR-150	Promotes megakaryocytopoiesis at the expense of erythropoiesis by targeting MYB	[17]
miR-34a	Enhances megakaryocytopoiesis of HSCs	[19]
miR-134,-139,-299-5p, -375,-409-3p,-132/212, -181a/b,-221/222	Upregulated only in megakaryocytopoiesis	[19]
miR-146a	1. Suppressed in and negatively regulates megakaryocytopoiesis and up-regulated in megakaryocytes differentiation 2. Inducted in megakaryocytes and down-regulated in megakaryocytes differentiation	[22], [23], [24], [25]
miR-28	Negative regulator of megakaryocytes differentiation by targeting E2F6 and exists only in platelets	[18]

Gatsiou A…Stellos K, Curr Vasc Pharmacol, 2012



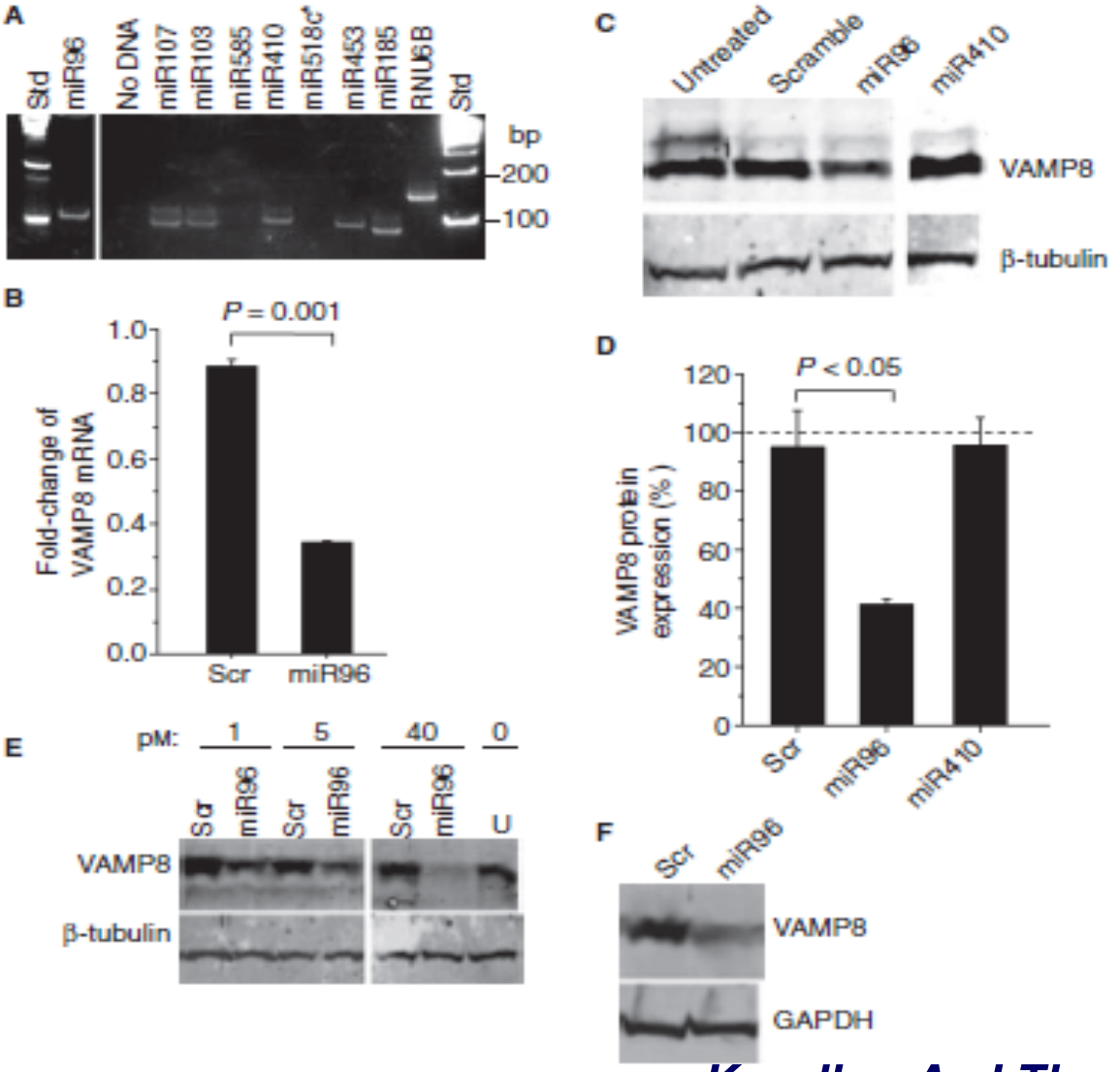
Gatsiou A…Stellos K, Curr Vasc Pharmacol, 2012 In Press

Platelet-bound P-selectin and extent of myocardial infarction



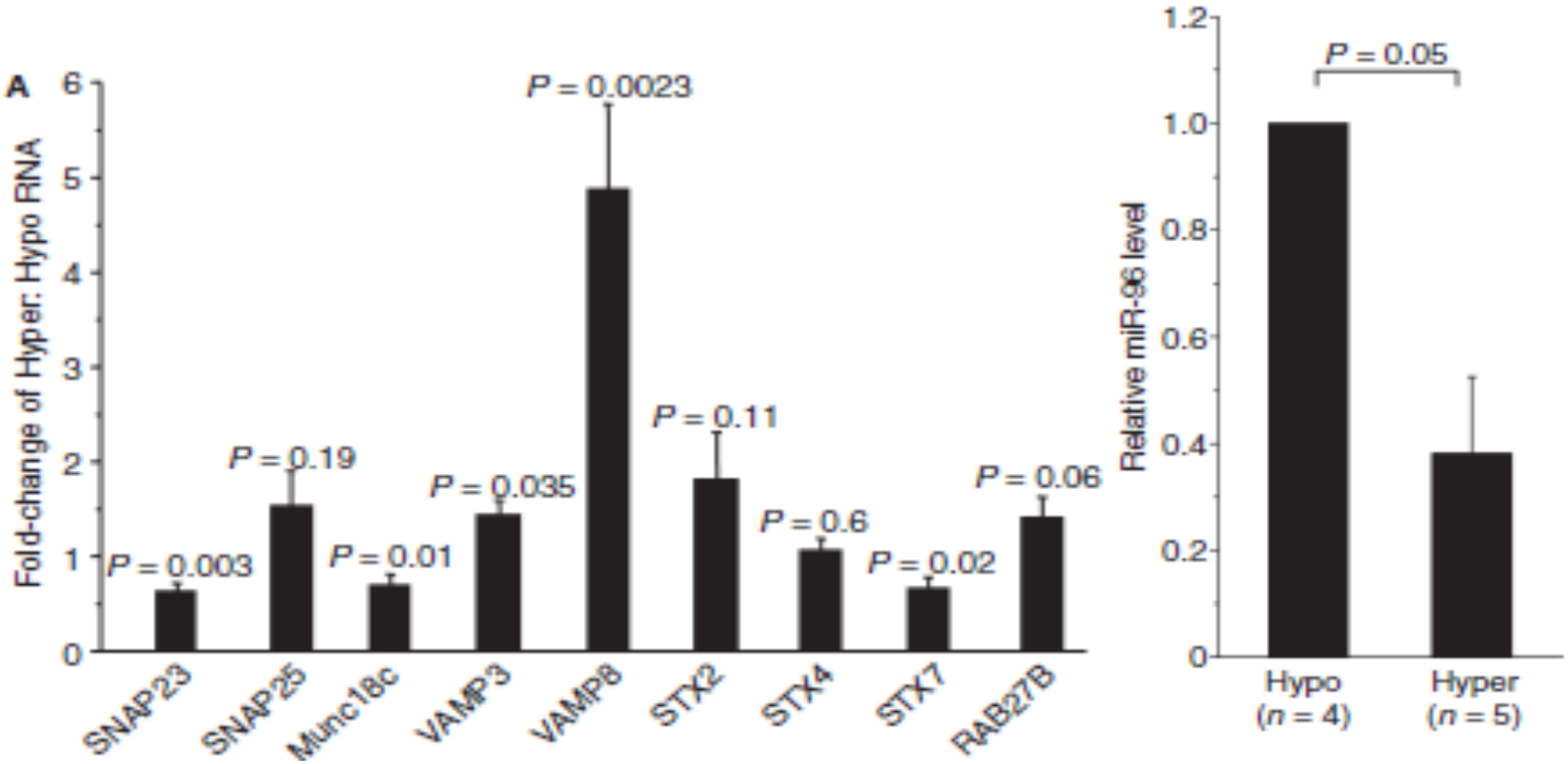
Stellos K, J Thromb Haemost, 2010

Platelet microRNA-96 inhibits platelet activation through VAMP8/ endobrevin pathway



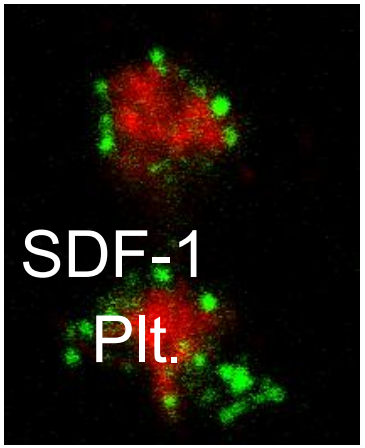
Kondkar A, J Thromb Haemost, 2010

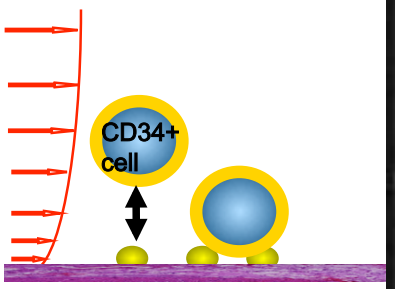
Platelet microRNA-96 inhibits platelet activation through VAMP8/ endobrevin pathway



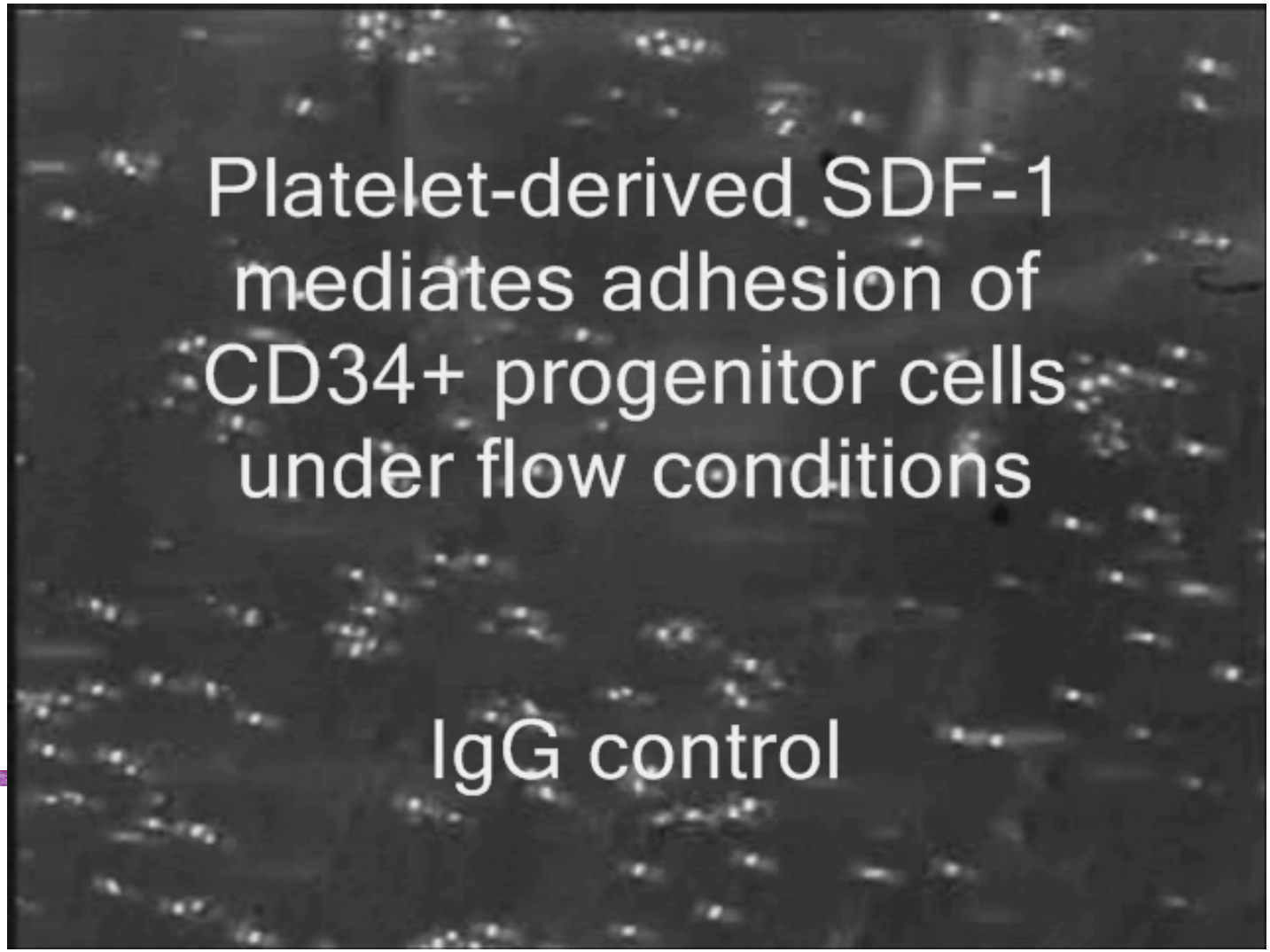
Kondkar A, J Thromb Haemost, 2010

Progenitor cell adhesion over immobilized platelets



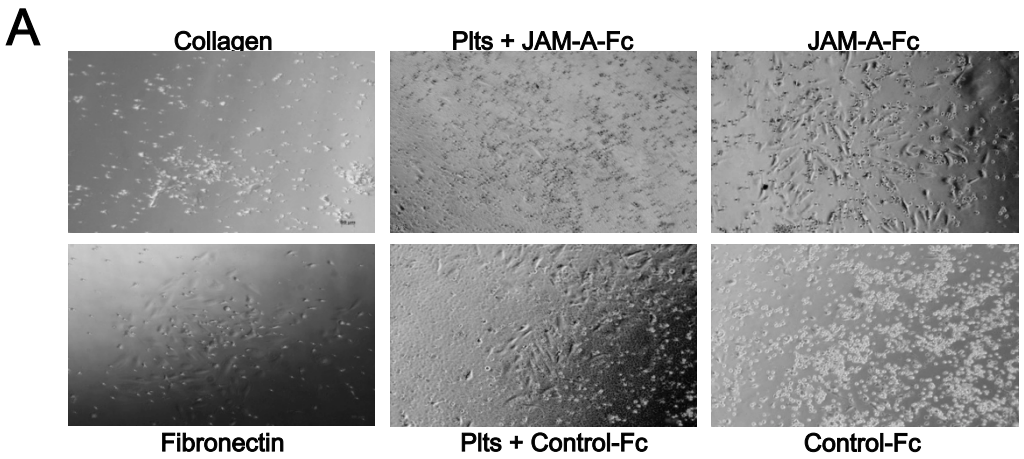


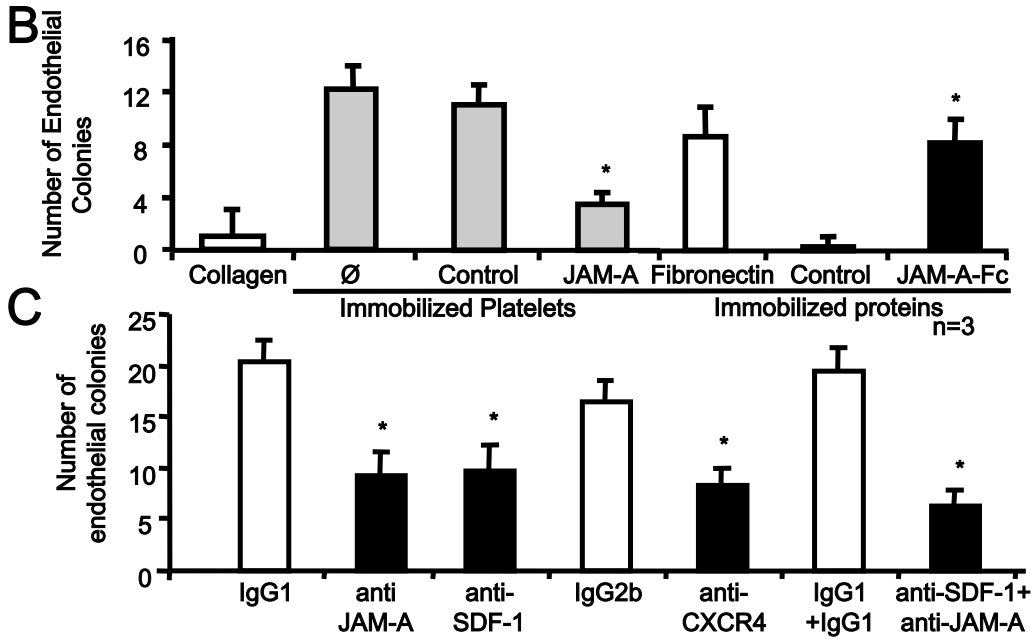
Flow Chamber

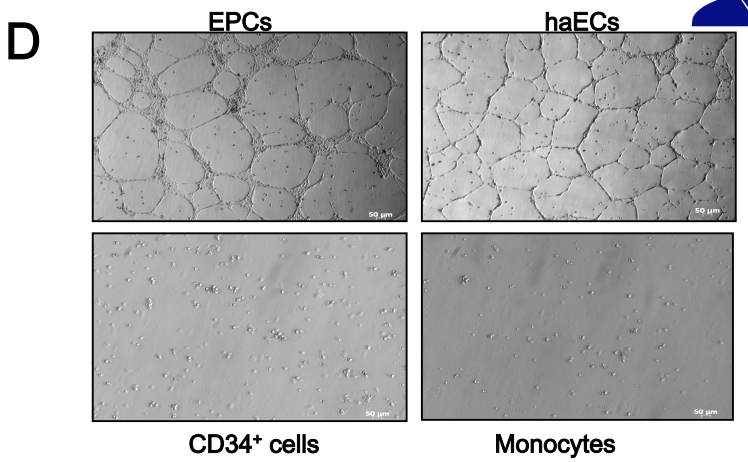


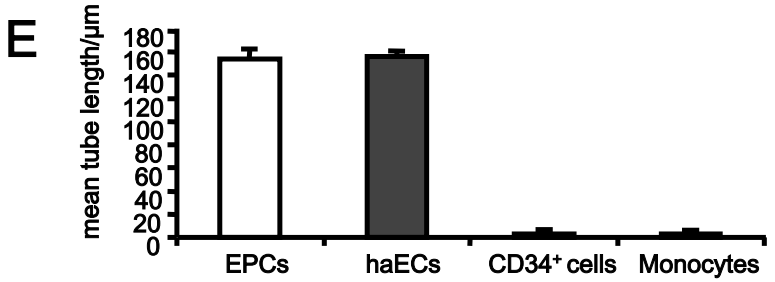
Stellos K, Circulation, 2008

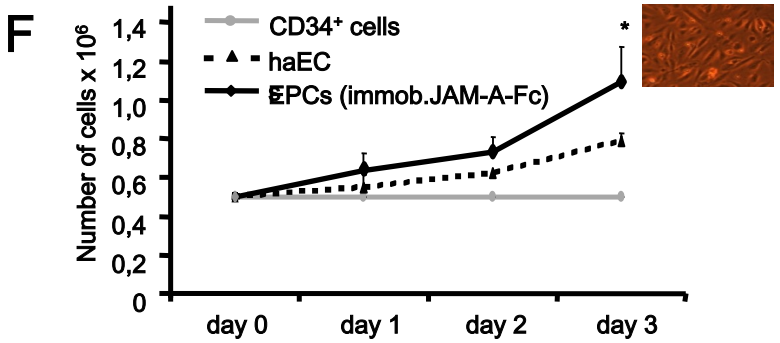
Platelet-derived SDF-1 and JAM-A regulate differentiation of CD34+ cells to late outgrowth proangiogenic cells





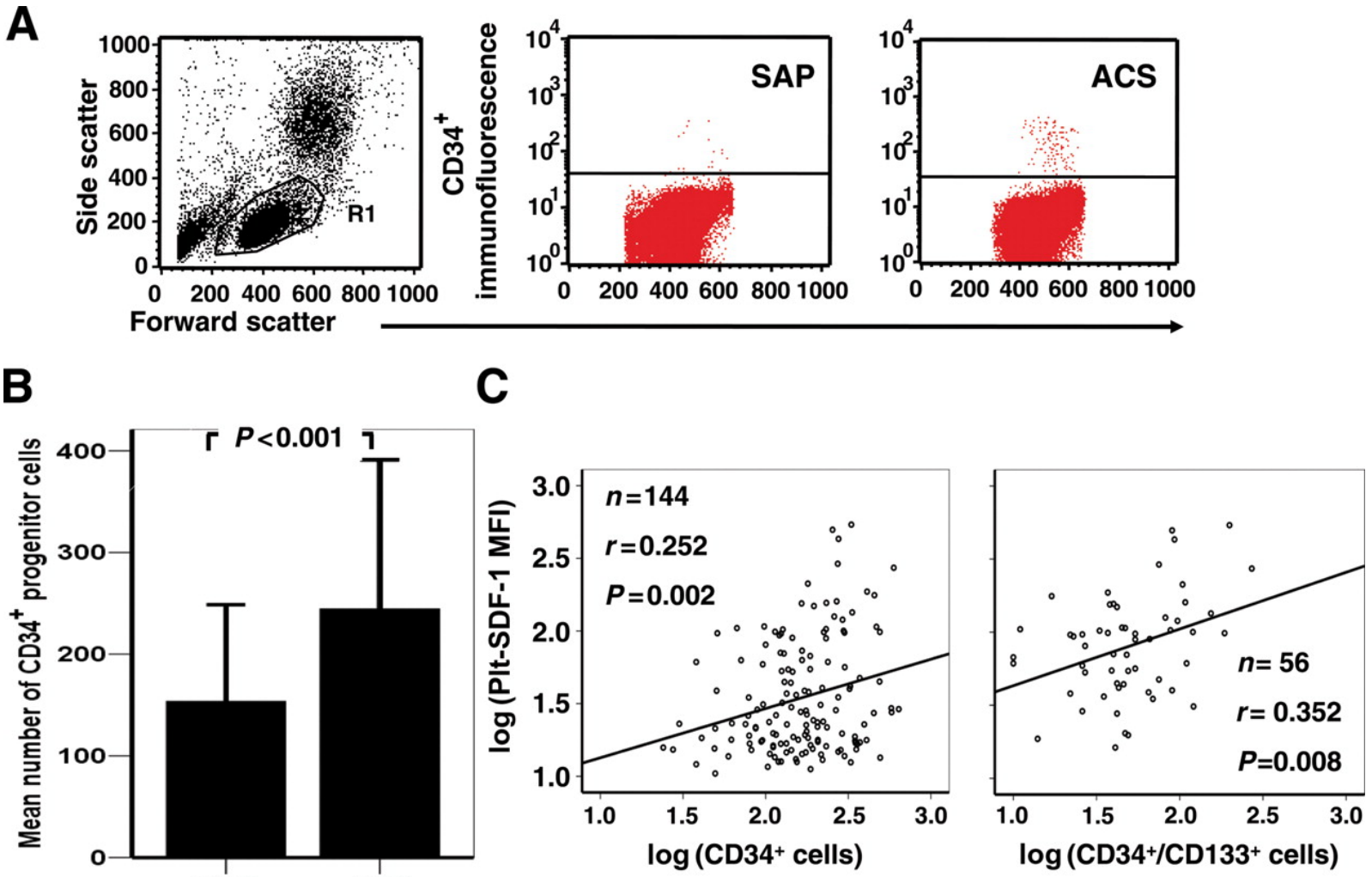






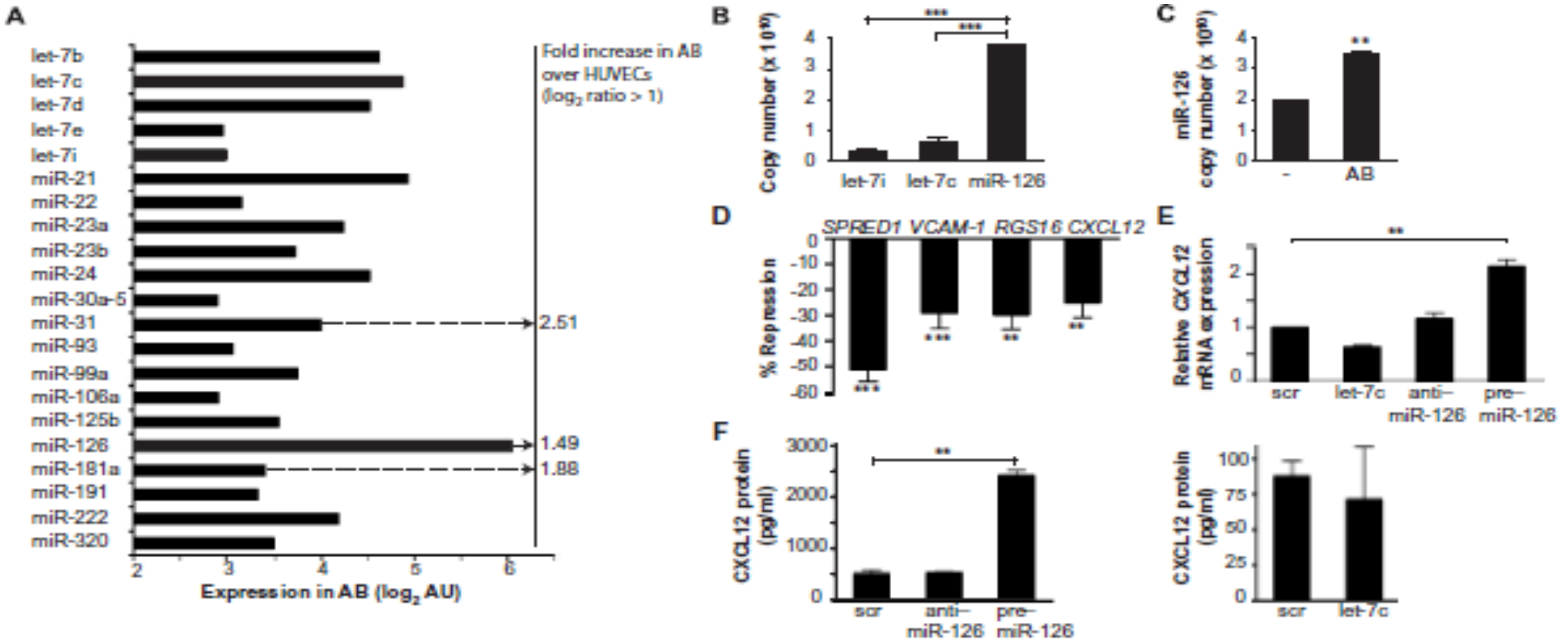
Stellos K, ATVB, 2010

Platelet-derived SDF-1 expression is increased in ACS and correlates with the number of CD34+ progenitor cells



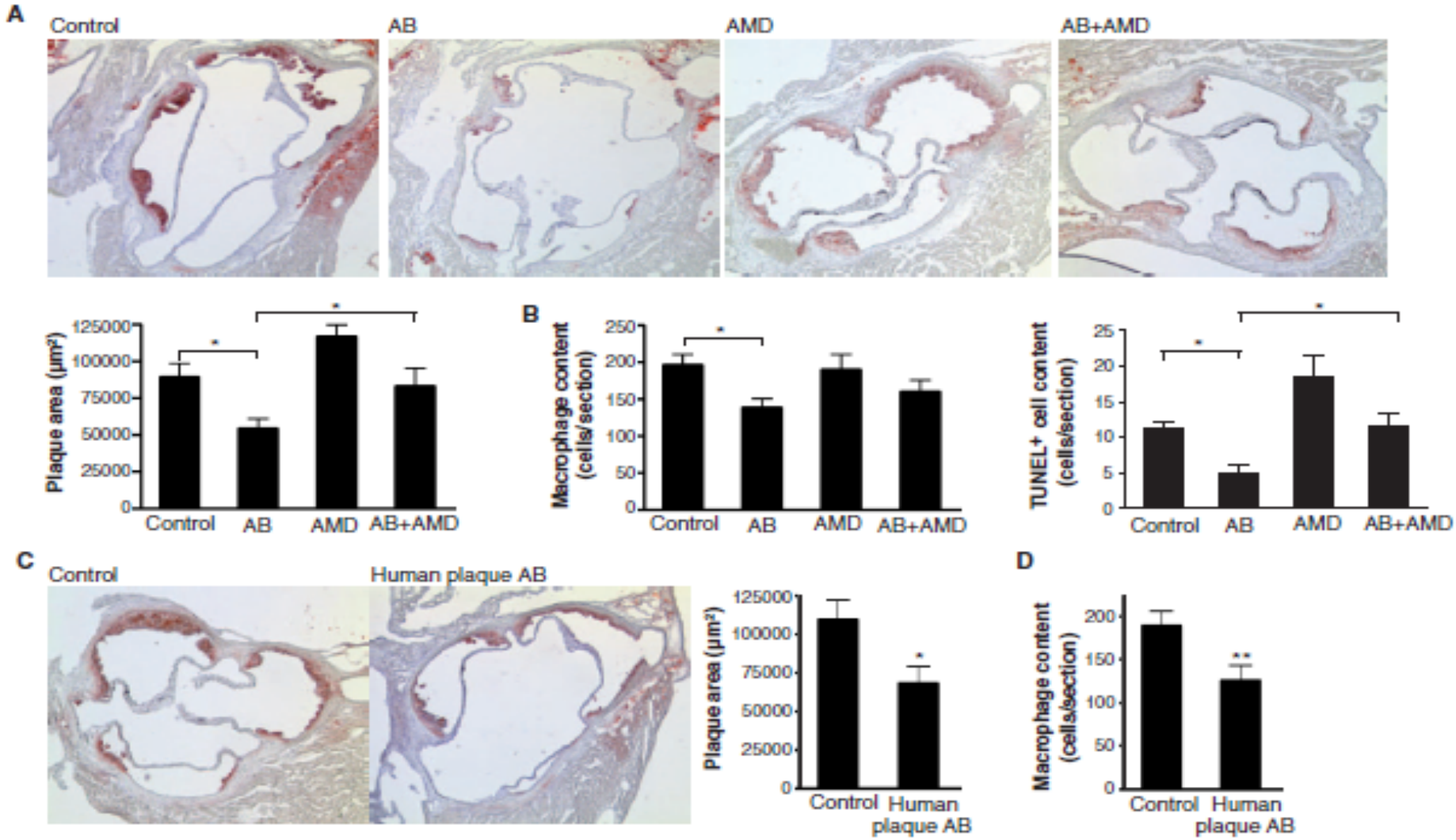
Stellos K, Eur Heart J, 2009

Apoptotic bodies carry miR-126 inducing SDF-1 Expression



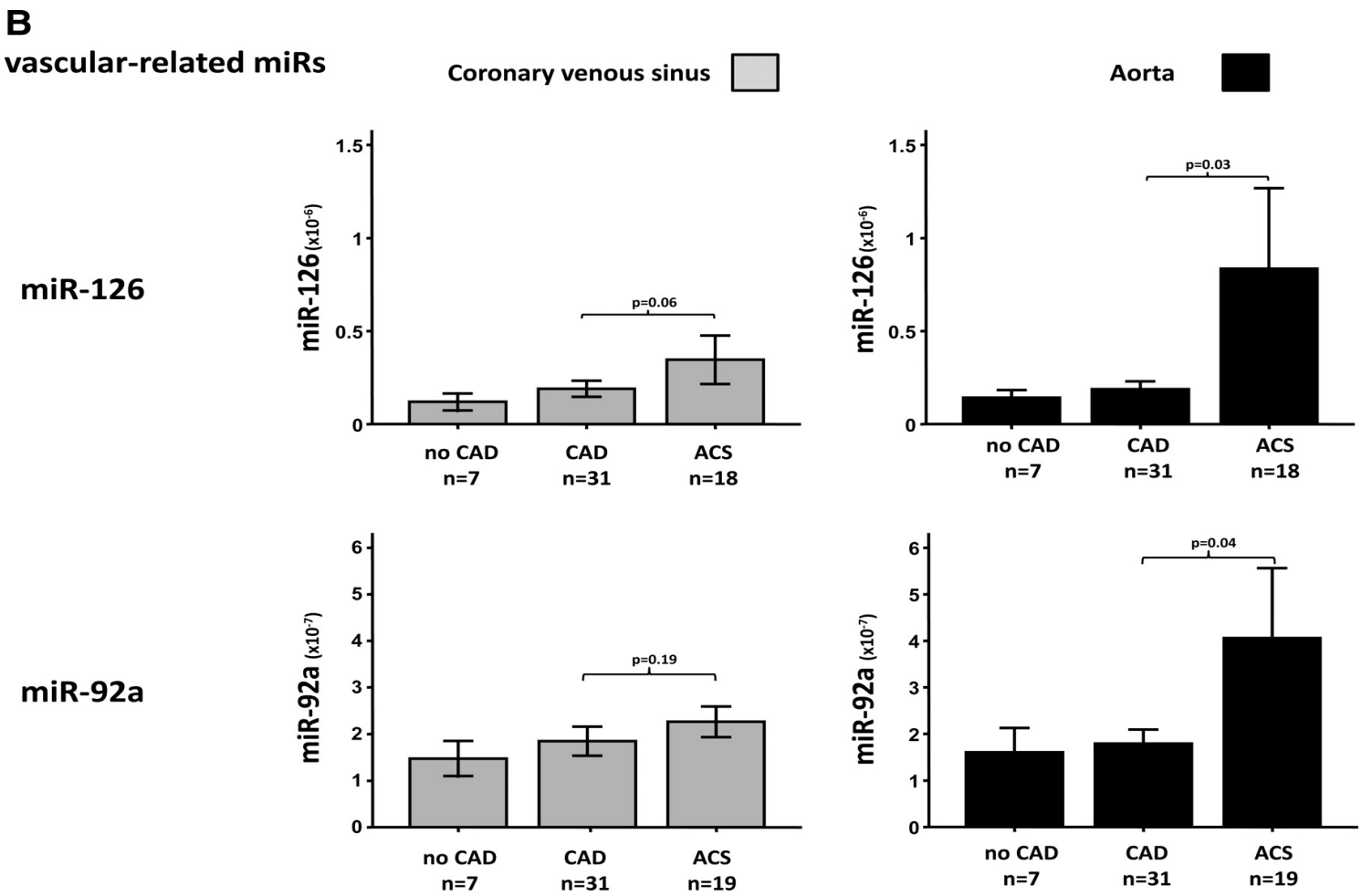
Zernecke, Sci Signal, 2009

Apoptotic bodies/miR-126/SDF-1 induction pathway protects against atheromatic plaque formation

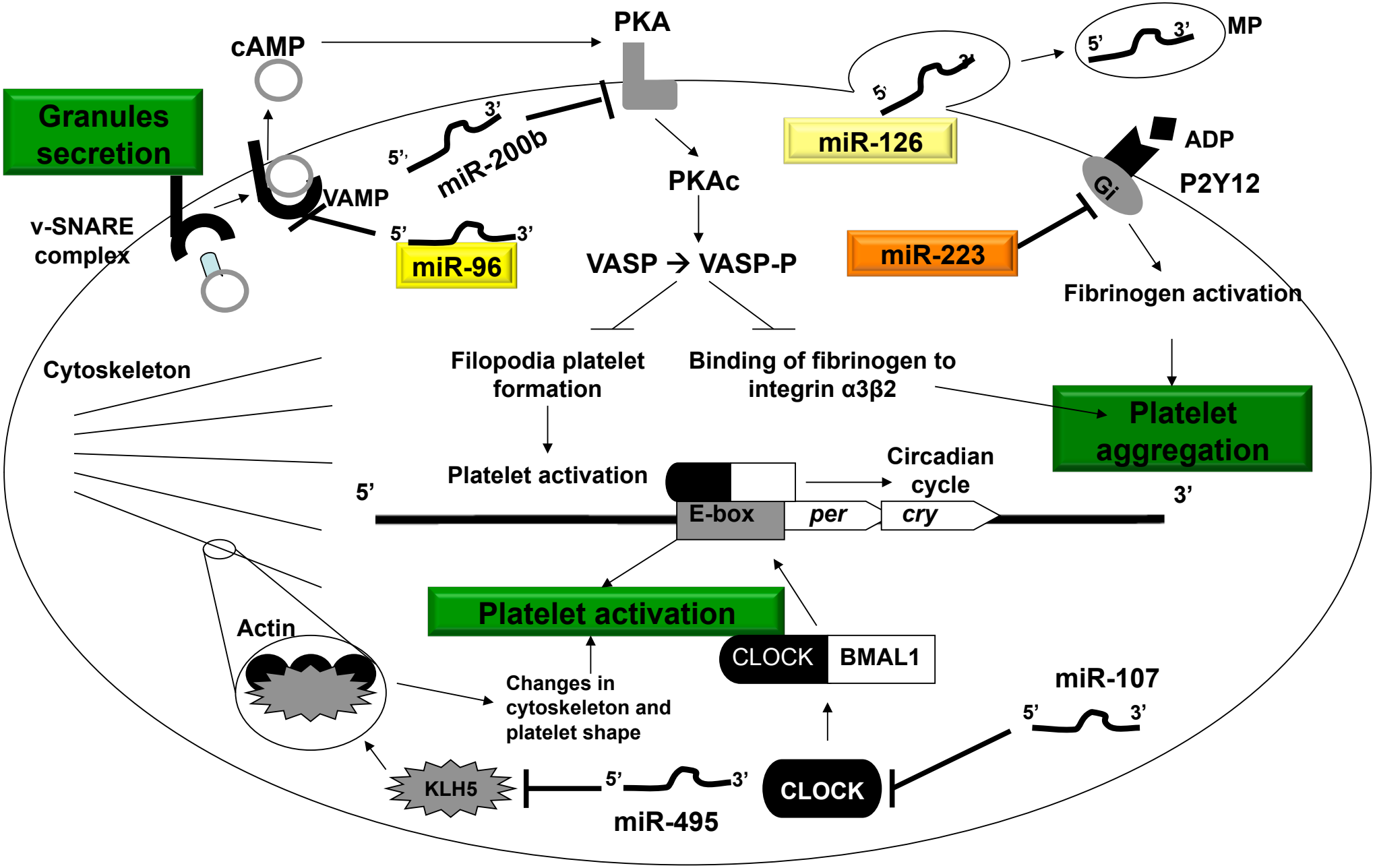


Zernecke, Sci Signal, 2009

Circulating microRNA (miR) levels in coronary sinus and aortic blood.



De Rosa S et al. Circulation 2011;124:1936-1944



Gatsiou A…Stellos K, Curr Vasc Pharmacol, 2012 In Press

Thank you!

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