

**Angiogenesis**

Angiogenesis is the physiological process by which new blood vessels are formed from preexisting blood vessels. Angiogenesis is a critical process in normal growth and development, wound healing, and repair, as well as in the formation of granulation tissue.

**CD34<sup>+</sup> cells**

CD34<sup>+</sup> cells are hematopoietic stem cells that express the protein CD34, which is also known as hematopoietic progenitor cell antigen CD34. CD34 is a protein identified by the cluster of differentiation nomenclature used to identify cell surface molecules, and it is a cell surface glycoprotein that has been shown to participate in cell-cell adhesion. Identification of CD34<sup>+</sup> cells is often used as a marker for activated hematopoietic stem cells.

**Framingham Heart Study**

The Framingham Heart Study was initiated in 1948 as a joint effort between the National Heart Institute (now the National Heart Lung and Blood Institute) and Boston College and is now the longest running prospective cohort study in the United States. The objective of the study was to identify risk factors for the development of cardiovascular disease over time in participants who had not yet developed cardiovascular disease or suffered myocardial infarction or stroke. The first generation of participants was enrolled in Framingham, Massachusetts in 1948; a second generation, in 1971; and a third generation, in 2002 and 2003. The Framingham Heart Study has contributed to the understanding of overall and cardiovascular mortality in the setting of various pathologies, including obesity, diabetes, and metabolic syndrome.

**Glycolysis**

Glycolysis is the series of biochemical reactions occurring in the cytosolic compartment that converts a glucose molecule into two molecules of pyruvate. In the presence of oxygen (ie, the aerobic setting), pyruvate is transported into the mitochondria and undergoes oxidative decarboxylation, yielding acetyl coenzyme A. In the absence of oxygen (ie, the anaerobic setting), pyruvate is reduced to lactate by the enzyme lactate dehydrogenase, which generates the nicotinamide adenine dinucleotide (NAD<sup>+</sup>) required to maintain flux through glycolysis.

**HbA<sub>1c</sub>**

Glycated hemoglobin (HbA<sub>1c</sub>) forms from the non-enzymatic coupling of glucose to the major component of adult hemoglobin (ie, HbA  $\alpha_2\beta_2$ ). Glucose, via a complex series of reactions, is coupled to specific valine residues of HbA  $\beta$  chains. HbA<sub>1c</sub> levels at a threshold of 6.5% can be used as a diagnostic test indicative of diabetes. HbA<sub>1c</sub> levels are reflective of average glycemic control over a period of 2 to 3 months before testing/analysis.

**I<sub>f</sub> current**

The funny current (*I<sub>f</sub>*), also referred to as a pacemaker current, is a hyperpolarization-activated inward current of mixed ionic nature (Na<sup>+</sup>, K<sup>+</sup>) that contributes to pacemaker activity in sinoatrial node cells (also atrioventricular node cells, and Purkinje fibers). The pore-forming subunits of the *I<sub>f</sub>* channel are formed by members of the hyperpolarization-activated cyclic nucleotide-gated gene family (HCN1-HCN4). As such, *I<sub>f</sub>* is responsive to changes in intracellular cyclic adenosine monophosphate (cAMP) levels in response to, for example, the activation of  $\beta$  adrenoceptors (increased cAMP) or M2 muscarinic receptors (decreased cAMP), and thus contributes to the basic physiological mechanisms mediating the effects of the autonomic nervous system on heart rate.

**Microvascular dysfunction**

Microvascular dysfunction (also known as small-vessel disease) occurs when damage arises in the walls and inner lining of the small coronary artery blood vessels that branch off from the larger coronary arteries (ie, left coronary artery). The damage in these smaller coronary artery blood vessels can produce spasms that decrease blood flow to the myocardium and thereby cause ischemia, and is more likely to develop in women.

**Silent ischemia**

Myocardial ischemia describes the situation where the heart/myocardium does not receive enough blood through the coronary circulation. The reduced blood flow and subsequent lack of oxygen delivery to the myocardium produces the sensation of chest pain, which is known as angina. If an individual does not experience the sensation of pain, it is referred to as "silent ischemia." Individuals who have experienced previous heart attacks or are diabetic are at increased risk for developing silent ischemia.

**TNF- $\alpha$** 

Tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) is a proinflammatory cytokine produced primarily by macrophages (also by other cells of the immune system, cardiac myocytes, adipocytes, fibroblasts, neurons). TNF- $\alpha$  is produced as a 216-amino-acid transmembrane protein arranged as homotrimers. The metalloproteinase, TNF- $\alpha$  converting enzyme (TACE/ADAM17) proteolytically cleaves transmembrane homotrimers, releasing soluble, 51-kDa TNF- $\alpha$  homotrimers. Both transmembrane and soluble TNF- $\alpha$  are biologically active, exerting effects via the activation of two receptor subtypes, TNFR1 (transmembrane, soluble TNF- $\alpha$  homotrimers) and TNFR2 (transmembrane TNF- $\alpha$  homotrimers).

**Variant angina**

Variant angina (also known as vasospastic angina) is a form of angina (sensation of chest pain) that occurs at rest in cycles. It is typically caused by a vasospasm, which is an arterial spasm that induces vasoconstriction of smooth muscle cells within the blood vessel wall, leading to myocardial ischemia.