

Fibroblast growth factors (FGFs)

FGFs are secreted glycoproteins, which are localized to the extracellular matrix by heparin sulfate proteoglycans. The activity of various heparinases, proteases, and FGF-binding proteins will release FGFs from the extracellular matrix, and then free FGFs can activate cell surface FGF receptors. FGF2 is the most characterized FGF and important paracrine factor involved in the development of cardiac hypertrophy.

Insulin-like growth factors (IGFs)

IGFs (IGF-1 and IGF-2) share sequence similarity with insulin. IGF-1 is an important mediator of the effects of growth hormone (GH). Secretion of GH increases IGF-1 secretion from the liver and local tissues, which, in turn, stimulates systemic body growth. In the heart, IGF-1 is an important regulator of physiological growth/physiological hypertrophy. Furthermore, IGF-1 may be implicated in heart failure where its circulating levels are decreased.

Monounsaturated fatty acids (MUFAs)

MUFAs are fatty acids that contain only one double bond in their carbon backbone. Oleic acid is one of the most important MUFAs because it circulates at the highest concentration in our body and is critical for energy metabolism.

Peroxisome proliferator-activated receptors (PPARs)

PPARs are members of the ligand-activated nuclear receptor superfamily. In mammals, three distinct PPAR isoforms have been identified (PPAR α , PPAR γ , and PPAR β /d) with differential tissue distributions. PPARs regulate the expression of various enzymes involved lipid metabolism by forming heterodimers with retinoid X receptors and binding

to PPAR response elements in the promoter region of target genes.

Polyunsaturated fatty acids (PUFAs)

PUFAs are fatty acids that contain more than one double bond in their carbon backbone. The essential fatty acids, alpha-linolenic acid (omega-3 fatty acid) and linolenic acid (omega-6 fatty acid) represent two of the most important PUFAs as they cannot be synthesized endogenously in our bodies.

Sirtuin proteins (SIRT6)

SIRT proteins are orthologues of the silent information regulator 2 (Sir2) gene family, which is conserved from bacteria to humans. SIRT6 are either class III histone deacetylases/NAD⁺-dependent lysine deacetylases (SIRT1, -2, -3, -5, -7) or ADP-ribosyltransferases (SIRT4, -6) with varying subcellular localization. SIRT6 have been implicated in regulating lifespan/longevity in lower organisms. They are also important regulators of a variety of processes in mammalian cells including signal transduction, cellular transport, gene transcription, and metabolism.

Trimethylamine-N-oxide (TMAO)

TMAO is an organic amine oxide, which is formed from the oxidation of trimethylamine and hydrogen peroxide via the catalytic activity of flavin monooxygenase. TMAO may act as an important osmoregulatory compound affecting buoyancy and potentially protecting protein function under high pressure in fish. Recent studies in animals and humans also suggest that TMAO may act as a proatherogenic compound, and elevated TMAO levels are positively associated with increased cardiovascular risk in both rodents and humans.