

## 세미나 초록

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발표 주제	Gut pathogen's last breath and host diseases: High-fat diet-induced intestinal inflammation links gut dysbiosis and cardiovascular disease
발표 내용	<p>A Western-style obesogenic diet, high in simple carbohydrates and saturated fatty acids, is associated with obesity, a condition that has reached epidemic proportions world-wide. A Western-style high-fat diet has been known to be associated with low-grade intestinal inflammation, gut dysbiosis and an increased risk for atherosclerosis. However, our knowledge about the pathways producing each of these different disease manifestations is incomplete, which makes it difficult to see connections. In my recent study, the question of which mechanisms drive changes in the gut microbiota composition during high-fat diet and whether the consequent dysbiosis increases the risk for cardiovascular disease was solved. Choline which is abundant substrate in high-fat diet is converted to trimethylamine (TMA) by the gut microbiota. However, whether diet-induced changes in intestinal physiology can alter the metabolic capacity of the microbiota remains unknown. Using a mouse model of diet- induced obesity, I found that chronic exposure to a high-fat diet escalates <i>Escherichia coli</i> (<i>E. coli</i>) choline catabolism by altering intestinal epithelial physiology. A high-fat diet impaired the bioenergetics of mitochondria in the colonic epithelium to increase the luminal bioavailability of oxygen and nitrate, thereby intensifying respiration-dependent choline catabolism of <i>E. coli</i>. In turn, <i>E. coli</i> choline catabolism increased levels of circulating trimethylamine <i>N</i>-oxide (TMAO), which is a potentially harmful metabolite generated by gut microbiota. This research provides innovation by establishing for the first time the molecular pathways connecting different major disease manifestations associated with high-fat diet.</p>