Autodigestion in Inflammation: Digestive Enzymes on the Prowl  
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Many diseases are accompanied by gastrointestinal co-morbidities but the molecular mechanism remains elusive. I will discuss two examples. Our evidence in acute experimental shock indicates, that the powerful pancreatic digestive enzymes, which are usually in the intestinal lumen, escape into the circulation at concentrations sufficient to cause autodigestion. The digestive enzymes activity degrades plasma proteins and membrane receptors and causes cell dysfunctions, organ failure and death. Blockade of digestive enzymes in the small intestine reduces autodigestion and morbidities in shock. In chronic cardiovascular disease unchecked proteases may also be present in the systemic circulation causing cell dysfunctions. We investigated the spontaneously hypertensive rat (SHR) with elevated blood pressure and diverse co-morbidities, e.g. insulin resistance, capillary rarefaction. SHR tissues, cells and plasma exhibit an unchecked extracellular proteolytic activity and extracellular domain receptor cleavage, causing reduced receptor functions. E.g. unchecked proteases cause cleavage of beta-2 adrenergic receptors and elevation of the SHR blood pressure. It also cleaves the insulin receptor with reduced insulin signaling (i.e. insulin resistance) and the VEGFR2s with endothelial apoptosis and loss of capillaries (i.e. rarefaction). The results suggest autodigestion may be a fundamental mechanism for cell/organ dysfunction, disease and death.