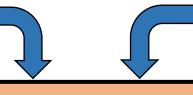
# Adipose-derived factors and diabetes-related factors

e.g. long-chain fatty acids, proinflammatory cytokines, decreased adiponectin, hyperglycemia, growth differentiation factor-15



### **NAFLD**

Steatosis
NASH
Liver fibrosis
& NAFLD-related Genotypes
(e.g. *PNPLA3, TM6SF2*)

#### **Intestine-derived factors**

e.g. diet (fructose), dysbiosis, endogenous alcohol production, modified bile acids, trimethylamine oxide, LPS, aromatic acid metabolites, p-cresyl sulphate, indoxyl sulphate, short-chain fatty acids, incretins

## Genetic factors and thrombogenic molecules

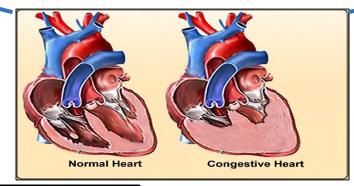
e.g. fibrinogen, transforming growth factor-beta, plasminogen activator inhibitor-1

### Insulin resistance and related disorders, activated RAAS

e.g. atherogenic dyslipidemia, hypertension, diabetes/prediabetes, chronic inflammation, noradrenaline

#### **Proinflammatory and oxidative stress factors**

e.g. interleukin-1 beta, interleukin-6, tumor necrosis factor-alpha, C-reactive protein, reactive oxygen species



Coronary microvascular dysfunction, cardiac remodeling (LV dysfunction or hypertrophy/fibrosis), cardiac autonomic dysfunction, CHD, certain arrhythmias



#### **Heart failure**