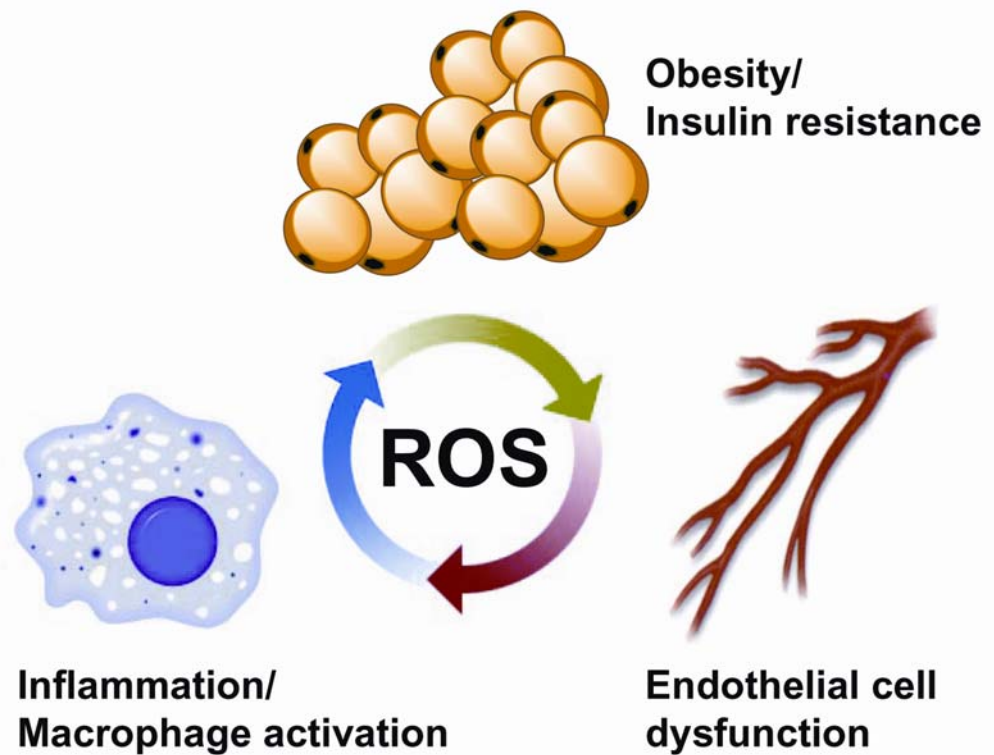


Cardiovascular Consequences of Metabolic Disease



Co-Directors:
Ken Walsh
Richard Cohen

ARC Participant List: 1st meeting (February 8, 2010)

Lei Wang
Fuzhang Qin
Jesse Lugus
Neil Ruderman
Joseph Vita
Mor L. Hartman
Melissa Farb
Wilson Colucci
Richard Cohen
Mengwei Zang
Sherman Bigornia
Bob Weisbrod
Hui Ping Zheng
Jennifer Parker
Kazuto Nakamura
Asish Saha
Tamar Aprahamian
Akiko Higuchi

Reiko Matsui
Nadia Kramer
Leon Li
Ei Ikegami
Tim Calamarns
Charlie Lee
Amber Giles
Rebecca Zee
Julia Xu
Lauren Nelson
Jose M. Caucedo
Melanie Mott
Keith Tornheim
Kenneth Walsh
Noriyuki Ouchi
Koji Ohashi

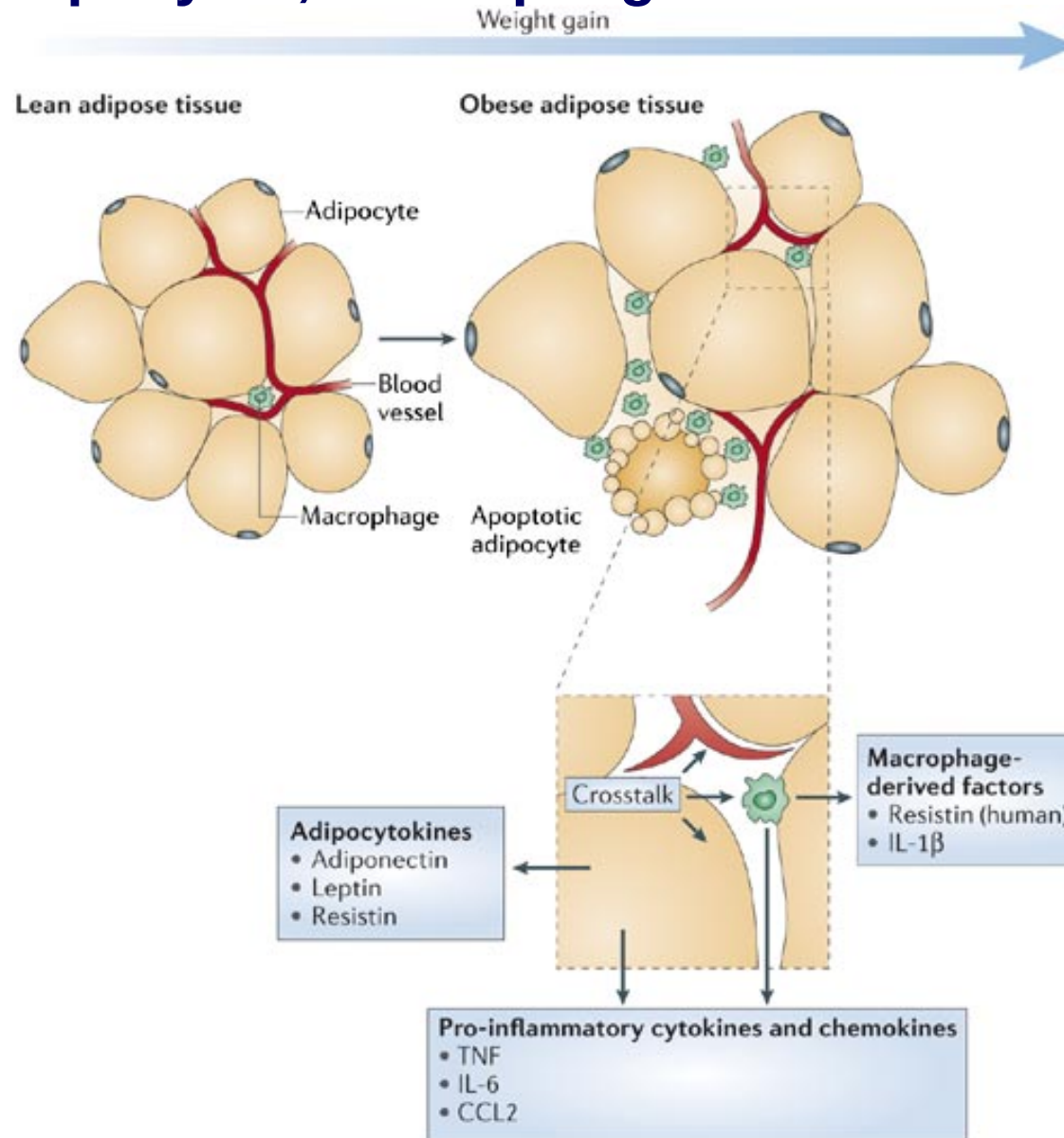
Cardiovascular Consequences of Metabolic Disease

Current resources:

3 program grants:

- AMPK, Endothelial Cell Dysfunction, and the Metabolic Syndrome
(PI Ruderman, Walsh, Cohen)
- Metabolic Control of Endothelial Cell Phenotype
(PI Walsh, Vita, Cohen, Gokce, Loscalzo)
- Vascular Consequences of Insulin Resistance and Obesity
(PI Vita, Gokce, Freedman, Hamilton)

Factors secreted from fat involved in crosstalk between adipocytes, macrophages and vascular cells



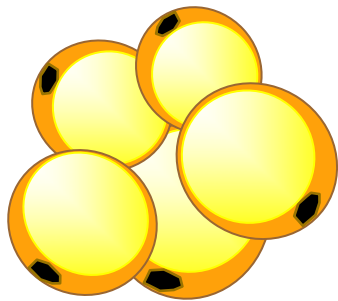
ARC Goals:

Foster cooperation between basic science and clinical labs investigating:

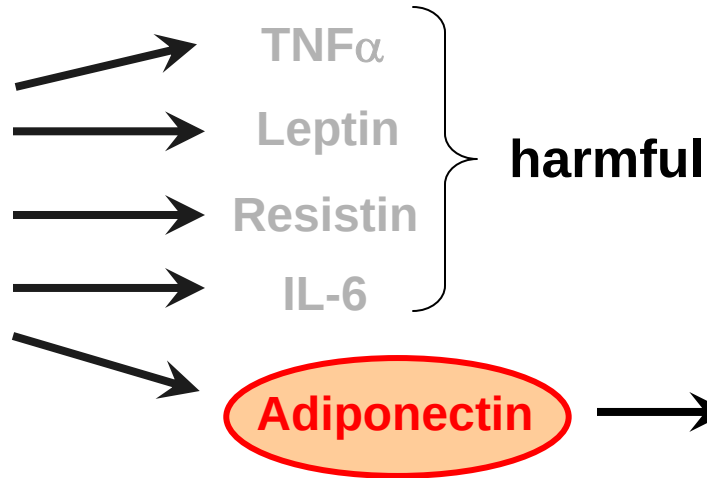
- 1) Fat as an endocrine organ
- 2) The vascular-protective effects of polyphenols (resveratrol); potential roles of Sirtuin-1, AMP kinase, and Adiponectin
- 3) The role of obesity-associated inflammation in microvascular dysfunction

Adipose tissue functions as an endocrine organ

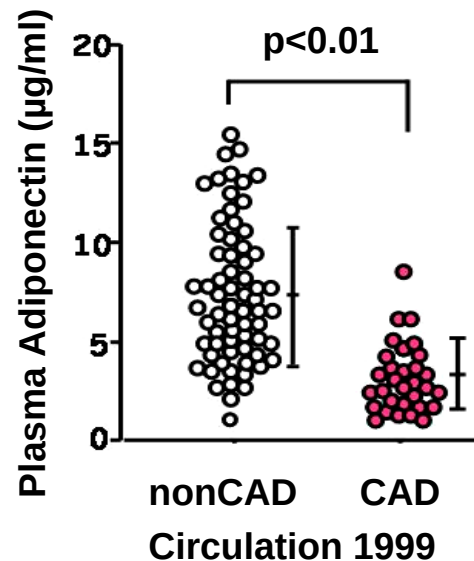
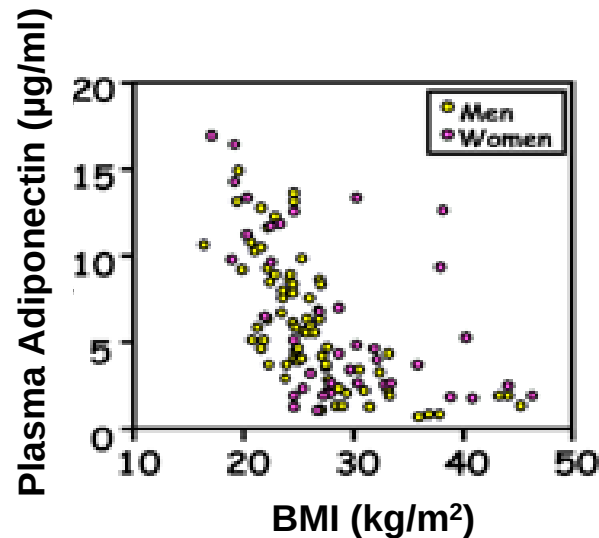
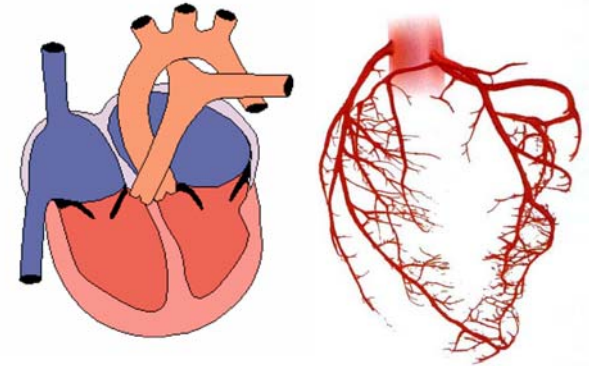
Adiposity



“Adipokines”



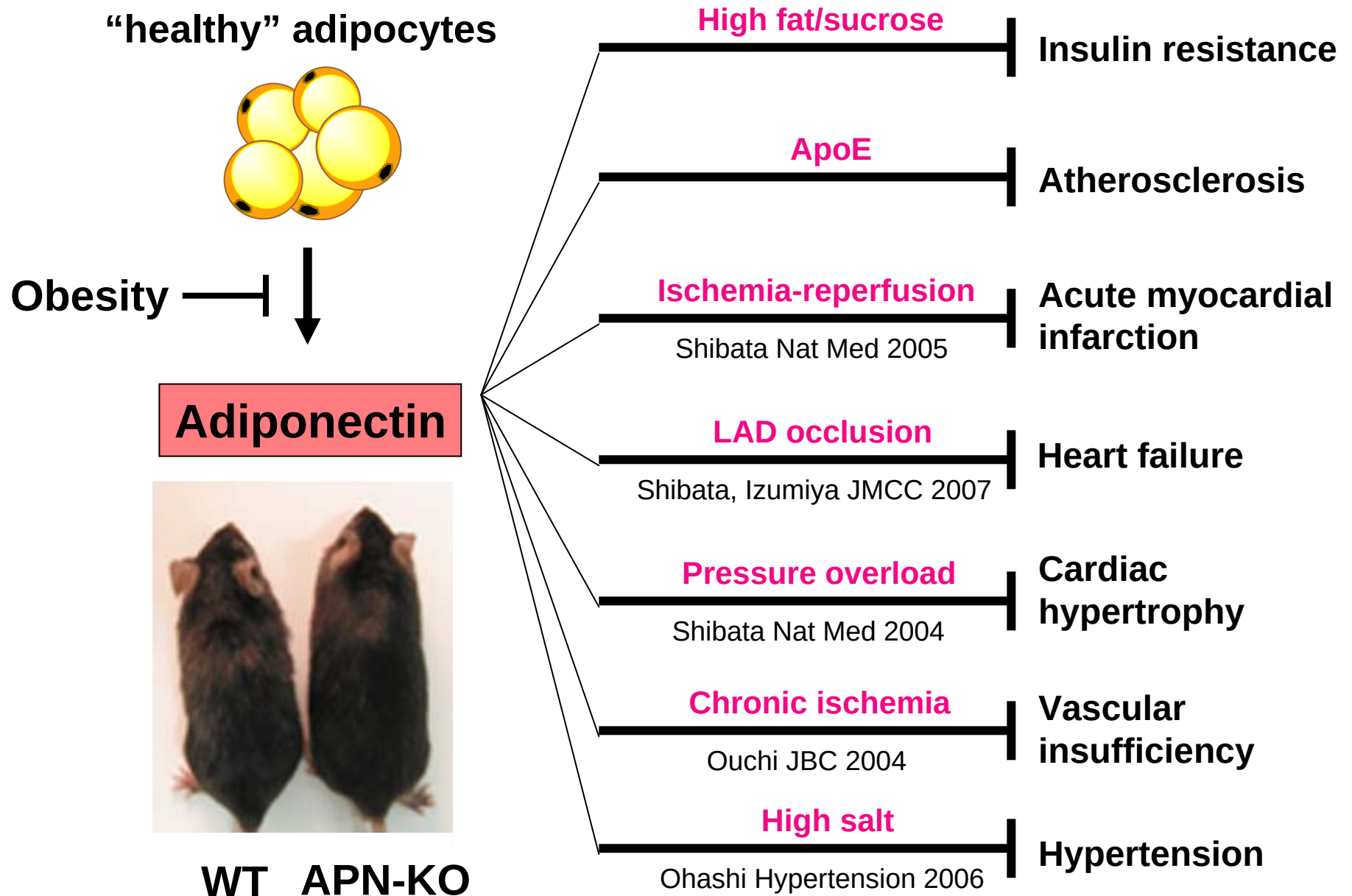
Cardiovascular disease



Hypo-adiponectinemia

- Coronary heart disease
- Type 2 diabetes
- Hypertension
- Stroke
- etc.

Adiponectin shows protective actions on obesity-linked metabolic and cardiovascular disease



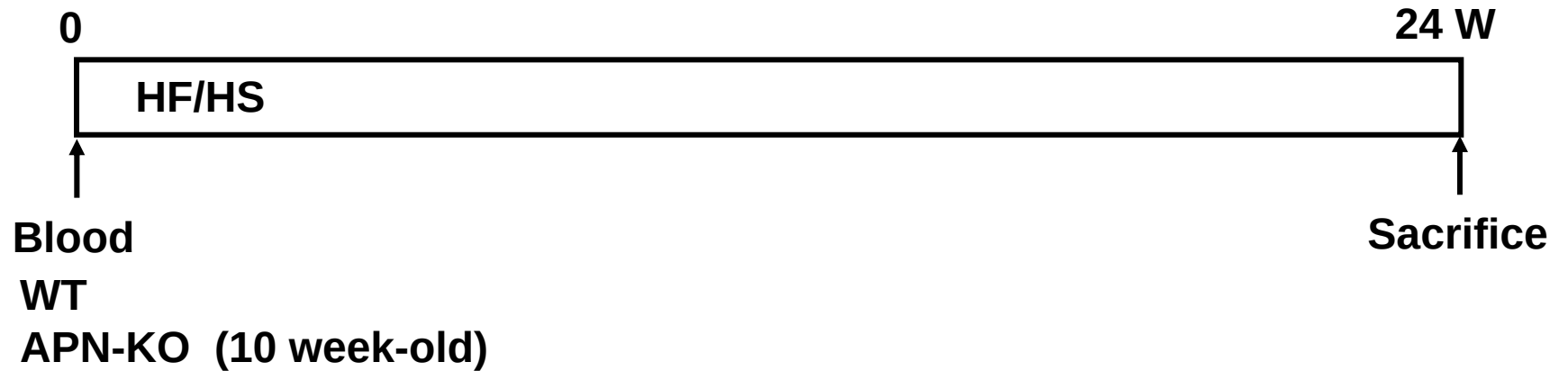
Preliminary studies:

Effects of resveratrol in WT and APN-KO mice fed a high calorie diet.

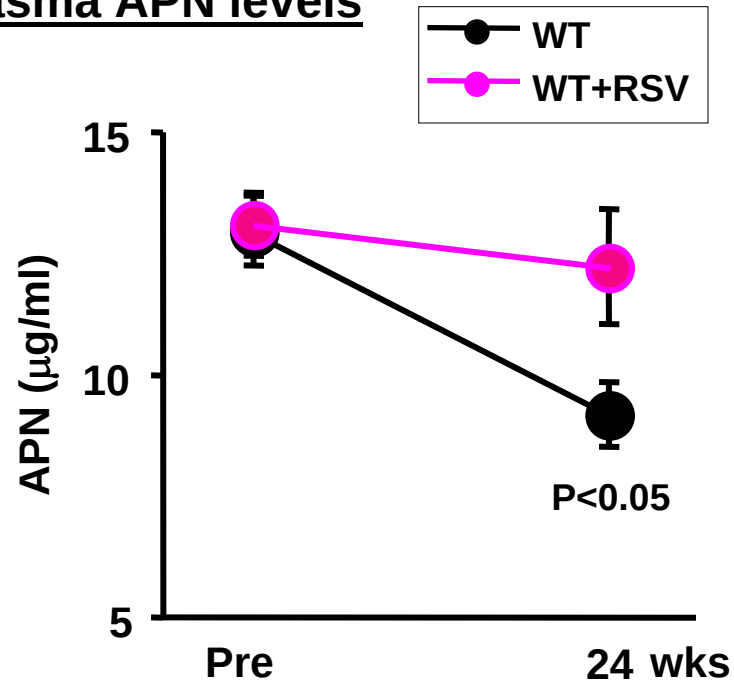
Treatment:	Resveratrol
Mice:	WT vs. APN-KO
Diet:	High fat / high sucrose

Ouchi/Walsh	- Metabolic measurements
Zang	- Liver
Colucci	- Cardiac function
Cohen	- Angiogenesis

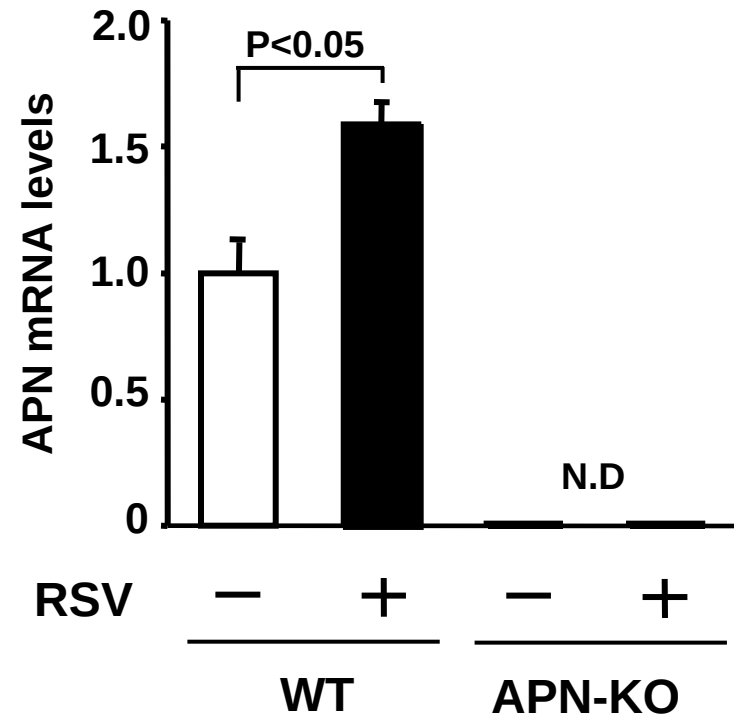
Changes in APN levels after treatment with RSV



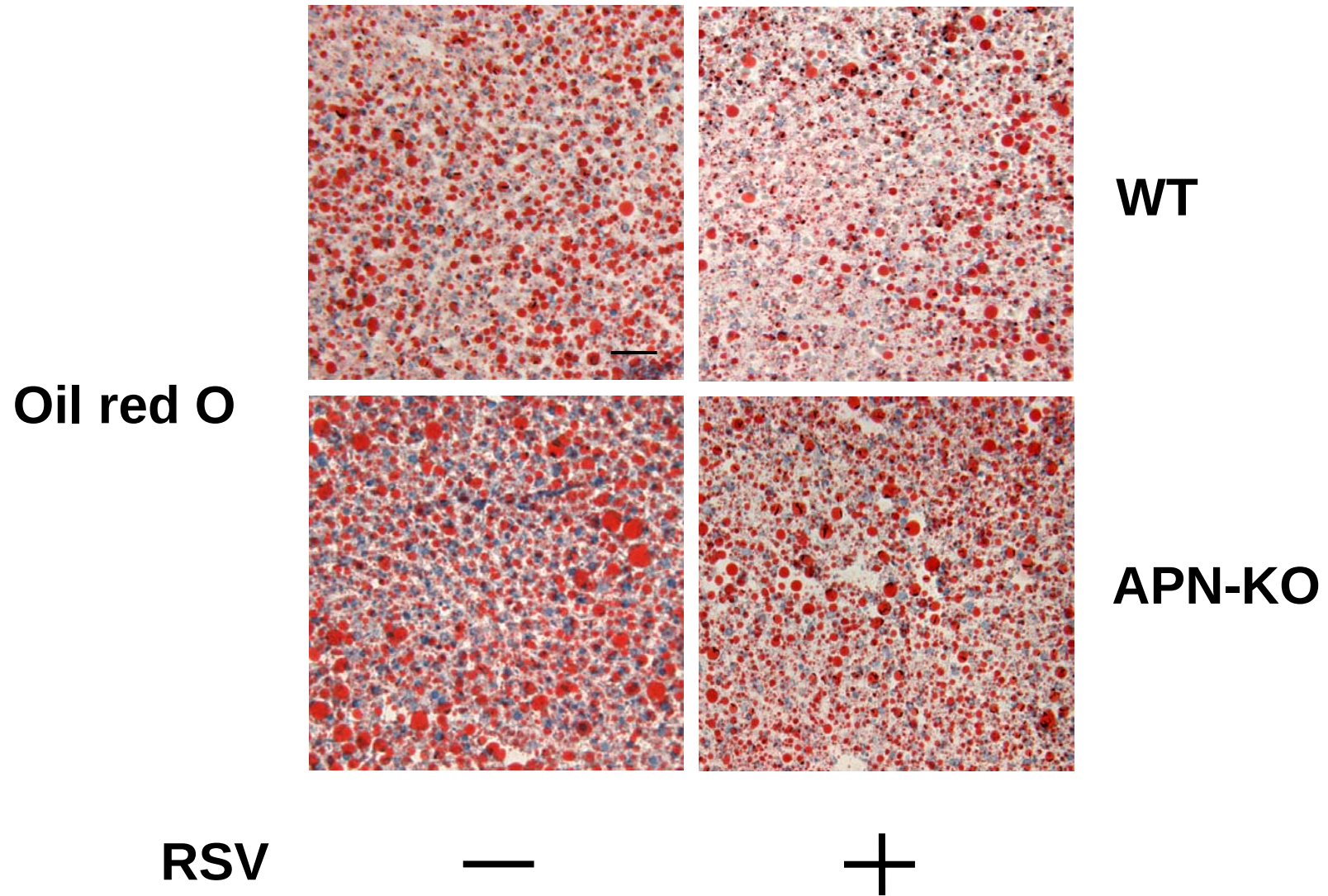
Plasma APN levels



APN mRNA in fat



Effect of RSV on lipid accumulation in liver



Questions raised/potential new directions

1. Control of adiponectin release from fat
(polyphenols, SIRT1, AMPK)
2. Adipokines: gene chip/proteomic analyses
3. Role of angiogenesis/hypoxia in fat on adiponectin release
4. Tissue effects of polyphenols (SIRT1, AMPK)
Liver, Heart, Angiogenesis, ?, ?