Fat Hormones and Energy Balance

Will Wong, Ph.D.
Associate Professor of Physiology
The Johns Hopkins University School of Medicine
The paradox of fat

Too much or too little is equally bad!
Problems with too much fat (obesity)

Artherosclerosis

Steatosis (fatty liver)

Diabetes

Cardiovascular disease
Problems with too little fat

Congenital Generalized Lipodystrophy

<table>
<thead>
<tr>
<th>Type</th>
<th>Gene</th>
</tr>
</thead>
<tbody>
<tr>
<td>CGI1</td>
<td>AGPAT2</td>
</tr>
<tr>
<td>CGI2</td>
<td>BSCL2</td>
</tr>
<tr>
<td>CGI3</td>
<td>Caveolin-1</td>
</tr>
<tr>
<td>CGI4</td>
<td>PTRF</td>
</tr>
</tbody>
</table>

- Severe diabetes
- Fatty blood
- Fatty liver
1. Major storage depot for fat

2. Secretes many hormones
Life without fat

Severe fatty liver
Severe diabetes

Moitra et al. (1998) Genes and Development
1. Major storage depot for triglyceride
2. Secretes many hormones
Three examples

- Leptin
- Adiponectin
- CTRP
Leptin: The first fat hormone

WT  ob/ob
Fat “talks” to the brain via leptin

Leptin

NPY, AgRP

POMC, CART

Neurons that promote eating

Neurons that suppress appetite

Net result: suppression of food intake
Reversal of obesity with leptin

Adiponectin
A fat-specific hormone
Massive expansion of fat tissue in \textit{ob/ob} mice overexpressing adiponectin

Dramatic reversal of diabetes in \textit{ob/ob} mice

Kim et al. (2007). \textit{JCI}.
CTRP hormones

(CTRP1-15)
Mice with more CTRP9 hormone are lean.
Overexpressing CTRP9 hormone reduces fat mass
CTRP9 Transgenic mice do not develop obesity when fed a high-fat diet.
Reversal of obesity in leptin-deficient mice

$ob/ob$

$ob/ob$

CTRP9 Tg

WT
Insulin sensitivity

Fat oxidation

Food intake

Body weight and energy balance

CTRP9
Current knowledge

How many fat hormones?
Adiponectin ↓
Leptin ↑
Omentin ↓
Vaspin ↓
Sfrp5 ↓
Zn-α2 glycoprotein (ZAG) ↓
Resistin ↑
RBP-4 ↑
Lipocalin-2 ↑
PAI-1 ↑
TNF-a ↑
MCP-1 ↑
IL-6 ↑
Chemerin ↑

Many more fat hormones…
The Challenge of Systems Physiology
END