Environmental PPARγ Agonists: What are they doing to our metabolic and bone health?

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Environmental PPARγ Agonists?

• PPARγ – a protein that controls fat formation. Fat is found under the skin, around the organs and in the bone marrow

• Agonists – turn on fat cell formation and fat storage programs by binding to PPARγ

• Where do we find PPARγ agonists? Everywhere!
PPARγ Agonists: Environmental Obesogens

Obesogens – toxicants that interfere with the ability to maintain a metabolic steady state

Prevalence of Obesity, 2011

A – chemical production
B – Percent overweight adults

Grun and Blumberg. 2006. Endocrinology
A high fat diet and obesogen exposure are a bad combination!

Organotins are used in:
- Antifouling agents
- Food crop fungicides
- Plastics

Schleizinger, unpublished data
Bone marrow: an unexpected but detrimental site of fat formation.

Normal bone

When fat is being made...

Osteoporotic bone

Bone is not!


Schlezinger, unpublished data
Prenatal exposure to Firemaster 550® is obesogenic... why?

Firemaster® 550 and Triphenyl Phosphate turn on PPARγ, increase fat formation and decrease bone formation.

What remains to be understood?

1. PPARγ agonists are used as therapeutics to treat type 2 diabetes... how then can exposure to environmental ligands be bad for metabolic health?
2. Therapeutic PPARγ ligands are known to increase fracture risk... can exposure to environmental ligands enhance the negative side effects of drugs?
3. What contribution could environmental exposures make to the expected increase in prevalence of low bone density and osteoporosis?
4. Can exposure to environmental PPARγ ligands not only increase our risk of fracture, but also compromise the ability of our bones to heal?
5. We are exposed to a complex milieu of environmental PPARγ ligands that are likely to be acting in concert to impact health... can we predict how those mixtures will impact metabolic and bone health?