



## Correspondence

## Paradoxical inflammation revisited: Muraglitazar and cardiovascular risk

A recent editorial in the Journal of the American Medical Association suggests that muraglitazar, a diabetes drug under development, may be associated with an unexplained increased rate of conditions associated with inflammation such as stroke and heart disease [1]. Muraglitazar acts through the binding of peroxisome proliferator-activated receptors (PPARs), specifically the PPAR- $\gamma$  family. In addition to modulating insulin sensitivity, activation of these receptors leads to an acute reduction in inflammation [2]. As we proposed earlier in the case of non-steroidal anti-inflammatory agents [3], a paradoxical host response to chronic muraglitazar use may produce compensatory increased levels of inflammation that would explain the heightened cardiovascular risk. Such paradoxical long-term sequelae have now arisen in two classes of drugs with entirely distinct mechanisms of action. This finding suggests that such effects may not necessarily arise from invoking specific functional pathways, but may originate instead from a more fundamental physiologic response – a conclusion that provides greater support for our hypothesis. Indeed, if we consider other agents with this conceptual framework in mind, we may find that this source of risk has existed and may still exist for many other medications. This para-

digm may highlight the need for significant changes in how we approach the temporal dimension of treatment.

## References

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- [3] Doux JD, Bazar KA, Lee PY, Yun AJ. Can chronic use of anti-inflammatory agents paradoxically promote chronic inflammation through compensatory host response. *Med Hypotheses* 2005;65(2):389–91.

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## Avian flu virus H5N1: No proof for existence, pathogenicity, or pandemic potential; non-“H5N1” causation omitted

WHO, CDC, Robert Koch Institute (RKI), and Friedrich Loeffler Institute (FLI) claim that H5N1

(avian flu virus) is “highly contagious”. Further, Reinhard Kurth, president of RKI, says that