Cell Surface Localization of ABCG1 Does Not Require LXR Activation

In Response:

Xie et al suggest that an alternative interpretation may explain the observation that LXR activation in macrophage preferentially presents ABCG1 at cell surface.1 They indicate that the newly synthesized ABCG1 on LXR activation may reach the cell surface through Golgi apparatus in macrophage, rather than via redistribution of preexisting ABCG1 from intracellular pools.

Our interpretation that LXR activation facilitates redistribution of ABCG1 from an intracellular pool to cell surface is mainly based on the observation that in mouse primary macrophage, LXR activation not only increases total and cell-surface ABCG1 but also decreases ABCG1 in fractions partially parallel to the distribution of Golgi markers.1 In addition, LXR activation leads to a more pronounced increase in cell-surface ABCG1 than the increase in total cellular ABCG1.1 We hypothesize that the newly synthesized ABCG1 on LXR activation may transport through this intracellular pool to reach the cell surface as well. Our interpretation is also consistent with the results from the functional assays for ABCG1 activity. Studies from Edwards' and our group demonstrate that in mouse primary macrophage in culture, ABCG1-promoted cholesterol efflux is largely dependent on LXR activation,1–3 even though there is still a fair amount of ABCG1 detectable in the basal state.1 Therefore, LXR activation may facilitate presentation of ABCG1 at cell surface in macrophage by both transcriptional and posttranscriptional mechanisms.

Although our data could not rule out the alternative interpretation proposed by Xie et al, several issues in the studies by Xie et al need to be considered. These authors used an overexpression system in cultured cells to test their ideas. As shown by several groups including ours, overexpression of native or N-terminally tagged ABCG1 in cultured cells results in cell surface presentation of ABCG1 without LXR activation.1,4 The data presented by Xie et al confirmed these earlier findings. However, the massive overexpression may not reflect the physiological regulation of cellular ABCG1 distribution in vivo. Indeed, the same authors reported previously that endogenous ABCG1 was mainly intracellularly localized in the basal state in macrophage with little cell surface staining.5

Disclosures

None.

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