Highlight on Mouse Endocan

To the Editor:

There are now emerging data involving the endothelial cell–derived human endocan as a key actor of the tumor progression. Little, however, is known about mouse endocan, until recently. Two novel reports, 1 from Circulation Research describing the effects of the genetic deletion of endocan on angiogenesis and inflammation and the other from Oncotarget describing specific biochemical and functional characters for mouse endocan lift the veil on how can mouse endocan act, unexpectedly not so similar to its human counterpart.

What Is Human Endocan?

Human endocan is a product of a unique gene called esm1. It circulates as a dermatan sulfate proteoglycan constituted of a mature polypeptide of 165 aminocids and a dermatan sulfate chain of 15 to 30 kDa O-glycanated on the serine 137. Endocan is overexpressed by specialized endothelial tip cells. It belongs to a set of 6 genes specifically overexpressed during the angiogenic switch. In human tumors, endocan is overexpressed by endothelial cells from various cancers such as non–small lung cancer, hepatocarcinoma, kidney cancer, glioblastoma, and bladder cancer. Multiple studies identified endocan expression as part of molecular signatures defining a poor prognosis in non–small lung cancer, breast cancer, glioblastoma, and hepatocarcinoma. In mice models of tumor xenografts, overexpression of human endocan induces tumor growth of nontumorigenic HEK293 (human embryonic kidney) cells and accelerate tumor growth of the tumorigenic HT-29 cells. Most of these effects have been attributed to the glycan moiety of endocan. It promotes vascular sprouting and vascular endothelial growth factor–induced migration of endothelial cells. In addition, endocan shows a potential anti-inflammatory activity through inhibition of the LFA-1 (leukocyte function antigen)–dependent leukocyte function, which could contribute to its net protumoral activity.

What Is Mouse Endocan?
The mouse endocan gene has been cloned first in our laboratory in 1999 (Genbank accession number AJ249354). It encodes for a mature polypeptide of 165 aminocids with 72% homology and conserved structural domains. Mouse endocan also circulates freely at ≈1 ng/mL. Consistently, mouse endocan was found expressed in endothelial tip cells from several retinal angiogenesis models. The Aird’s group demonstrated overexpression of mouse endocan by tumor endothelial cells in xenogenic tumors, but they also found that mouse endocan is spontaneously produced by nonendothelial cells from lung, kidney, and spleen.

Using endocan knockout mice, Rocha et al reported recently in Circulation Research that endocan is required for optimal response to vascular endothelial growth factor (less endothelial filopodia and less cerebral edema in knockout mice). Interestingly, endocan was shown to increase the recruitment of leukocytes 2 to 4 hours after intraperitoneal injection of interleukin-1β. More recently, Yassine et al reported in Oncotarget that mouse endocan is much less glycanated than its human counterpart. Surprisingly, the non–glycanated endocan seems to favor the recruitment of leukocytes into the experimental solid tumors.

Both Rocha’s and Yassine’s reports support the idea that the main circulating form of endocan in healthy mice is nonendothelial and nonglycanated, different from the main human circulating form, which is endothelial-derived and full glycanated. Each of these forms has potential opposite biological properties depending on its glycanic status: protumoral and anti-inflammatory for the glycanated form; antitumoral and proinflammatory for the non-glycanated form.

Mouse endocan sounds more complex than its human counterpart. Several unanswered questions remain. Quid on the glycan status and the function(s) of the true endothelial cell–derived endocan overexpressed by vessels from experimental tumors? Which common pathways endocan uses in the so different clinical contexts like inflammation or cancer? A fascinating exploratory domain is now open which could conduct to the control of tumor progression by regulating inflammation.

Disclosures

None.

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(Circ Res. 2015;116:e69-e70. DOI: 10.1161/CIRCRESAHA.115.306353.)
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Circulation Research is available at http://circres.ahajournals.org

DOI: 10.1161/CIRCRESAHA.115.306353


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doi: 10.1161/CIRCRESAHA.115.306353

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