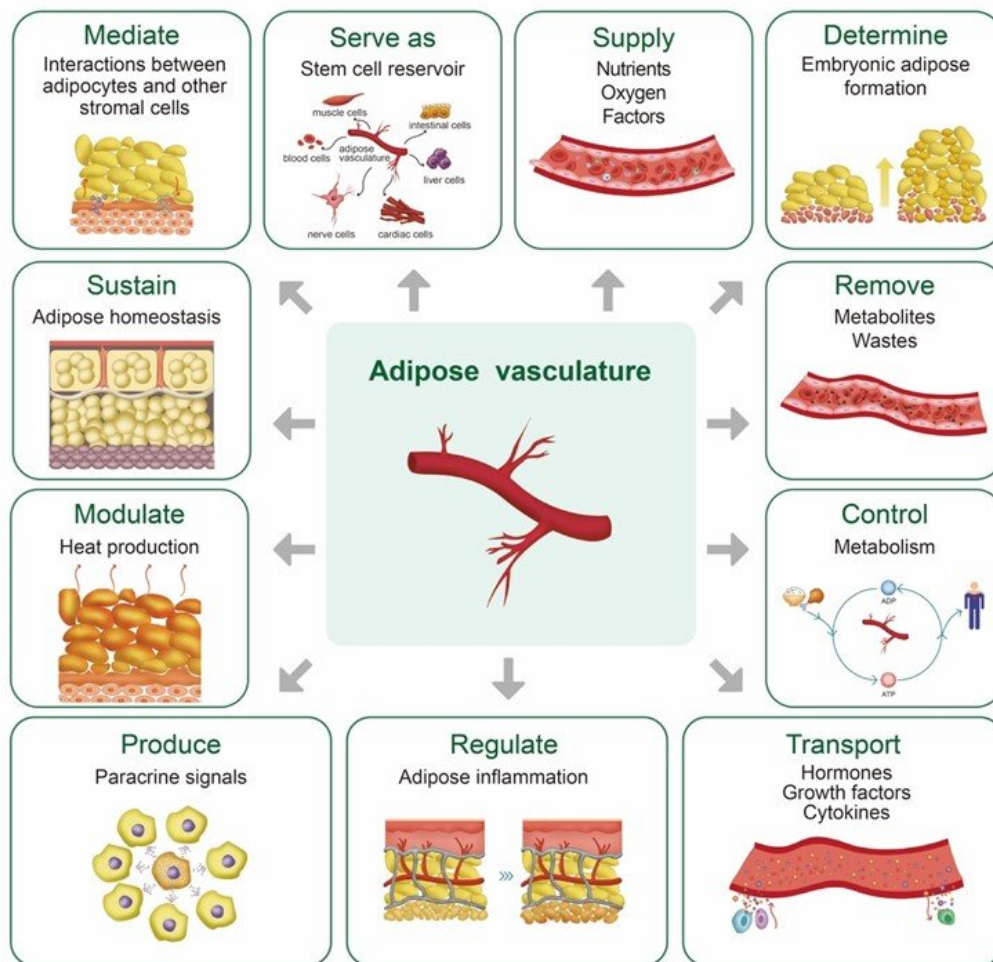


Probing the role of blood vessels in treating obesity-related disorders

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The adipose vasculature executes a range of important functions including the development of adipocytes, supply of oxygen and nutrients to adipocytes,

regulation of heat production by adipocytes, etc. Credit: Yihai Cao

Diabetes and its associated consequences are a major health concern around the world. They lead to significant mortality. For instance, type 2 diabetes mellitus (T2DM) caused 1.5 million deaths in 2019. Of the various factors contributing to T2DM, obesity is a leading one.

Obesity primarily leads to alterations in adipose tissues, a type of connective tissue in the body that is associated with fat accumulation. Incidentally, there are two types of adipose tissues with distinct functions—[white adipose tissue](#) or WAT, which stores energy in the form of lipid droplets in the fat cells, and [brown adipose tissue](#) or BAT, which releases energy in the form of heat by lipid breakdown.

As it turns out, these adipose tissues are extensively enveloped by [blood vessels](#), which have diverse roles including supply of oxygen and nutrition to the adipose tissue, development of the tissue, and regulation of lipid metabolism.

Recently, these blood vessels and their association with adipose tissues have garnered much attention in connection with metabolic disorders. Now, in an article, Professor Yihai Cao, of the Karolinska Institute, Sweden, has summarized the regulatory roles of blood vessels in adipose tissue functioning, and highlighted the associated therapeutic implications.

Discussing the motivation behind the review, Prof. Cao says, "Obesity-associated metabolic disorders such as type 2 diabetes have become a global pandemic. The incidences of metabolic diseases continue to rise and have become a major threat to human health. Targeting the blood vessels may prove to be effective in the treatment of diabetes and other

metabolic diseases." His short review has been published on November 16, 2022 as an editorial in the latest issue of the *Chinese Medical Journal*.

Prof. Cao's article suggests that although both WAT and BAT are densely surrounded by blood vessels, BAT, in particular, is profusely vascularized because it executes highly demanding metabolic functions including thermogenesis or heat generation.

Apart from BAT, the browning of WAT (bWAT), in recent times, has also received attention because it may have implications in obesity-related disorders. Interestingly, as Prof. Cao's article suggests, vascularization—the formation of blood vessels from precursor cells—plays a crucial role in mediating the browning of WAT.

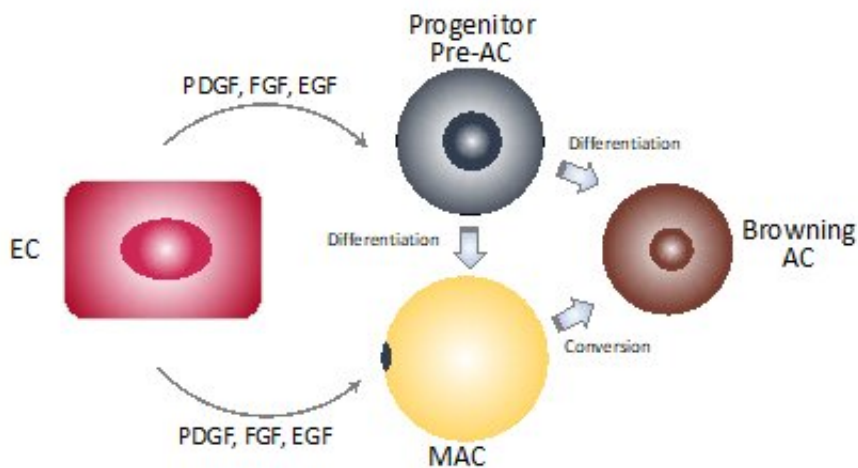
An important factor in this regard is the vascular endothelial growth factor receptor 2 (VEGFR2), produced by the vascular endothelial cells that form the inner lining of blood vessels. This receptor, in turn, stimulates the release of signaling molecules like platelet-derived growth factors (PDGFs) from the endothelial cells. Consequently, PDGFs promote the maturation and browning of adipocytes.

Given the plethora of roles vascularization plays in adipose tissue functioning, angiogenesis, or the formation of new blood vessels from pre-existing vessels, may provide a possible gateway for treating obesity, suggests Prof. Cao. Indeed, angiogenesis is beginning to show promise in the therapeutic domain.

However, the therapeutic implications are complex and multifactorial. While in certain contexts, stimulation of angiogenesis may help in treating obesity, in other cases its inhibition is helpful. For instance, studies show that inhibition of angiogenesis by an angiogenic inhibitor, TNP-470, facilitates weight loss in genetic mouse obese models. On the contrary, stimulation of angiogenesis by the targeted delivery of

angiogenic factors like VEGF helps in WAT and bWAT metabolism, and is, therefore, instrumental in obesity treatment.

Similarly, for diseases associated with obesity, like [diabetic retinopathy](#), an eye disorder induced by diabetes, it is useful to block angiogenesis because vascularization is an underlying cause of the disease. Certain other conditions like [diabetic foot ulcers](#) are treated by promoting angiogenesis, which thereby facilitates wound healing. Together, these findings point to a contextual role of vascularization, which should be an important consideration in therapeutics development.



Growth factors such as PDGF, FGF, EGF, released by vascular endothelial cells in response to angiogenic stimuli like vascular endothelial growth factors, mediate the maturation of adipocytes. Credit: Yihai Cao

Taken together, in this short review, the author has comprehensively charted the intricate interplay between blood vessels and adipose tissues in connection with obesity-associated [metabolic disorders](#). This

comprehensive overview could help further research into developing drugs that target blood vessels as an effective treatment for metabolic diseases.

Prof. Cao is hopeful about this potential targeting of angiogenesis in disease contexts. "Drugs targeting blood vessels are already available for treating diabetes-associated complications such as diabetic retinopathy. I strongly believe that in the future, more effective drugs with this principle will be developed. It can become one of the key therapeutic modalities within the next 5-10 years or so," he concludes.

More information: Yihai Cao, Blood vessels in fat tissues and vasculature-derived signals in controlling lipid metabolism and metabolic disease, *Chinese Medical Journal* (2022). [DOI: 10.1097/CM9.0000000000002406](https://doi.org/10.1097/CM9.0000000000002406)

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