**A Method for Regulating Angiogenesis through Modulation of ApoB**

**Methods of Regulating Angiogenesis by Administering Agents Which Modulate ApobB-100 Polypeptide Levels**

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| **Project Number:** | 1621 |
| **Principal Investigator:** | Dr. Karina Yaniv |
| **Patent Status:** | Pending |

**Overview**

**A novel method for treating cancer and other non-neoplastic diseases by inhibiting angiogenesis through regulating the levels apolipoprotein B (ApoB)**

**Background and Unmet Need**

Angiogenesis is the formation of new blood vessels from pre-existing vasculature. Therefore, angiogenesis is a fundamental part of tissue development. However, angiogenesis is also an important mechanism for the growth and metastasis of tumors. Tumor cells promote angiogenesis by secreting the signaling molecule VEGF (vascular endothelial growth factor) which binds to its respective receptor (VEGFR). Previous studies have shown that the vascular endothelial growth factor receptor 1 (VEGFR1) plays an inhibitory role in angiogenesis, acting as a “sink” for the VEGF ligand. **Therefore, inhibiting angiogenesis by VEGFR1, can be used as a potential method of retarding tumor progression.**

**The Technology**

The technology is based on the novel discovery, made in the lab of Dr. Karina Yaniv, that ApoB-containing lipoproteins regulate angiogenesis by elevating expression levels of VEGFR1. The team were also able to prove that the ApoB protein itself, and not the lipid moieties within the lipoprotein, acts on endothelial cells to regulate angiogenesis. Therefore by either increasing the amount of available apoB (e.g. by directly administering it) or by reducing apoB levels (e.g. adminstraing anti-apoB antibodies) one can suppress or promote angiogenesis respectively.

***Advantages and Applications***

* A novel orthogonal method for treating pathological angiogenesis.
* Diagnosis of metastasized cancer by determining the levels of apo-B in a fluid sample (blood, plasma, saliva, urine, etc.)
* Repressing angiogenesis by directly adminstraing ApoB.

**Development Status**

The team of Dr. Yaniv have demonstrated *in vivo* in zebrafish models the effects of ApoB-containing lipoproteins on angiogenesis. Using this model they have shown that exogenous delivery of LDL inhibits angiogenesis. *In vitro,* treating human aortic endothelial cells (HAECs) and human umbilical vein endothelial cells (HUVECs) with LDL elicited an increase in VEGFR1 expression. The team have also shown in hyperlipidemic and Apoe-negative or Ldlr-null mice increased endothelial-specific VEGFR1 expression compared to control *WT* mice, confirming the connection between ApoB and VEGFR1 expression in higher vertebrates. This research has been published in the prestigious scientific journal of *Nature Medicine[[1]](#footnote-0)*.

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1. Avraham-Davidi, Inbal, et al. "ApoB-containing lipoproteins regulate angiogenesis by modulating expression of VEGF receptor 1." *Nature medicine* 18.6 (2012): 967. [↑](#footnote-ref-0)