

Indication of vascular endothelial growth factor binding components from herbal extracts by Herbo Chip: A platform for drug screening on a chip

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Received date: November 25, 2021; Accepted date: December 01, 2021; Published date: December 10, 2021

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Introduction

Herbo Chip is an array of different fractions deriving from herbal extracts, which could be applied in drug screening. Here, we aimed to identify effective components from traditional Chinese medicines (TCMs) that interact with vascular endothelial growth factor (VEGF) as a target using Herbo Chip. The extracts of TCMs were chemical standardized and fractionated by a standard HPLC profiling. The biotinylated-VEGF was hybridized with chips coated with different HPLC-separated fractions from the herbal extracts. Straptavidin-Cy5 was used to identify the VEGF-bound fractions. Over 100 chips were screened, and 8 positive hits were identified. The interaction of identified herbal extracts/phyto-compounds with VEGF was further confirmed in cultured human umbilical endothelial cells. As a result, the identified herbal extracts/compounds interfered (i.e. binding) with VEGF-induced cell proliferation and cell migration. The amounts of phosphorylated eNOS, phosphorylated Akt and phosphorylated ERK 1/2 were markedly altered in the co-application of the herbal extracts/compounds with VEGF. In addition, the phosphorylation of eNOS, Akt and ERK 1/2 could be modulated by the identified extracts/compounds. Six compounds from TCMs showed activating activities on the VEGF response, and two TCM compounds showed inhibiting activities. In conclusion, the current result supported the applicability of HerboChip for screening VEGF binding components from herbal extracts.

HerboChip is an array of different fractions deriving from herbal extracts. This study aimed to identify effective components from Chinese medicine (CM) that interact with nerve growth factor (NGF) as a target using HerboChip. Fifty types of CM that are traditionally used as remedies for

emotion imbalance were selected and extracted with 50 % ethanol. Biotinylated-NGF was hybridized with over 300 chips coated with different HPLC-separated fractions from CM extracts and straptavidin-Cy5 was used to identify the NGF-bound fractions. Vascular endothelial growth factor (VEGF), originally known as vascular permeability factor (VPF), is a signal protein produced by many cells that stimulates the formation of blood vessels. To be specific, VEGF is a sub-family of growth factors, the platelet-derived growth factor family of cystine-knot growth factors. All members of the VEGF family stimulate cellular responses by binding to tyrosine kinase receptors (the VEGFRs) on the cell surface, causing them to dimerize and become activated through transphosphorylation, although to different sites, times, and extents. The VEGF receptors have an extracellular portion consisting of 7 immunoglobulin-like domains, a single transmembrane spanning region, and an intracellular portion containing a split tyrosine-kinase domain.

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