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PII: S0005-2736(18)30103-2
DOI: doi:10.1016/j.bbamem.2018.03.023
Reference: BBAMEM 82748

To appear in:

Received date: 8 January 2018
Revised date: 19 March 2018
Accepted date: 20 March 2018

Please cite this article as: Christopher King, Daniel Wirth, Samuel Workman, Kalina Hristova , Interactions between NRP1 and VEGFR2 molecules in the plasma membrane. The address for the corresponding author was captured as affiliation for all authors. Please check if appropriate. Bbamem(2018), doi:10.1016/j.bbamem.2018.03.023

Interactions between NRP1 and VEGFR2 molecules in the plasma membrane

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ABSTRACT

Here we use a quantitative FRET approach, specifically developed to probe membrane protein interactions, to study the homo-association of neuropilin 1 (NRP1) in the plasma membrane, as well as its hetero-interactions with vascular endothelial growth factor receptor 2 (VEGFR2). Experiments are performed both in the absence and presence of the soluble ligand vascular endothelial growth factor A (VEGFA), which binds to both VEGFR2 and NRP1. We demonstrate the presence of homo-interactions between NRP1 molecules, as well as hetero-interactions between NRP1 and VEGFR2 molecules, in the plasma membrane. Our results underscore the complex nature of the interactions between self-associating receptors, co-receptors, and their ligands in the plasma membrane. They also highlight the need for new methodologies that capture this complexity, and the need for precise physiological measurements of local receptor surface densities in the membrane of cells.

INTRODUCTION

Neuropilin 1 (NRP1), a 140 kDa transmembrane receptor, plays a critical role in the development of the embryonic cardiovascular and nervous systems (1, 2). NRP1 is a single pass membrane protein with a N-terminal extracellular region encompassing two CUB (complement C1r/C1s, urchin embryonic growth factor and bone morphogenic protein 1) domains, two domains that are homologous to coagulation factors V and VIII and are important for VEGFA-165 binding, and a MEM (meprin, A5, and receptor protein-tyrosine phosphatase μ) domain, which is proximal to the