acid-derived oncogenic lipid messengers that promote cancer cell migration and invasiveness. hMGL is a membrane proximal protein that belongs to the serine hydrolase family involved in the endocannabinoid signaling system (ECBSS). As a major part of the ECBSS that is composed of two main cannabinoid receptors CB1 and CB2 and endogenous ligands, hMGL exclusively hydrolyzes 2-arachidonoylglycerol (2-AG), making it a particularly critical modulator for the endocannabinoid transmission. hMGL also plays important roles in the metabolism of lipid storage. The key roles of hMGL in tuning homeostatic ECBSS and in supporting aggressive tumorigenesis make this protein a promising therapeutic target for treating cancer as well as managing brain and treating inflammatory, neurodegenerative, and immunological disorders. Using a custom built device that allows simultaneous surface plasmon resonance (SPR) and electrochemical impedance spectroscopy (EIS) measurements in real-time, we report for the first time, that hMGL introduces significant defects into pre-formed, intact, tethered phospholipid bilayer membranes (tBLMs) composed of phosphatidylcholines and other lipids. To probe the mechanism of hMGL’s ‘destructive activity’ to tBLMs we investigated wild-type and mutant hMGLs with respect to concentration, inhibitors, and pH. Our data shows that MGL’s lid domain, lytic activity center, and hydrophobic pocket all play important roles in this process.

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Effect of Lipid Composition on the Affinity and Binding of Dimeric Tubulin to Membranes Studied using Surface Plasmon Resonance, Neutron Reflectivity, Electrophysiology, and AC Electrical Methods
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Dimeric tubulin has emerged as an important regulatory factor of the permeability of voltage-dependent anion channel (VDAC) in the mitochondrial outer membrane, with implications for mitochondrial energetics as well as the Warburg effect observed in cancers. Previously, single-channel studies revealed that the on-rate of the VDAC-tubulin interaction is strongly dependent on the lipid environment. To understand the nature of the binding of this abundant cytosolic water-soluble protein to lipid membranes, we have employed an array of biophysical techniques using unsupported planar lipid membrane and tethered bilayer lipid membrane (tBLM) platforms. Surface plasmon resonance (SPR) of tBLMs shows that tubulin at concentrations less than 100 nM binds irreversibly to DPhPC and 1:1 DOPC:DOPA membranes. The binding rate is significantly larger in high salt concentrations, suggesting a hydrophobic interaction between tubulin and lipid membrane. No binding to DOPC membranes is observed under the same conditions. Electrochemical impedance spectroscopy (EIS) of tBLMs reveals that only DPhPC membranes are strongly perturbed by the binding of tubulin. Neutron reflectivity (NR) measurements on tBLMs give structural information regarding the penetration of the tubulin into the membranes. Electrophysiological measurements of the tubulin/VDAC interaction on the unsupported bilayers confirm the irreversibility of tubulin binding to DPhPC membranes and membranes with significant DOPC content. Second harmonic analysis of planar lipid membranes’ response to acoustic excitation suggests that tubulin binding causes significant rearrangements of the lipid headgroups. We conclude that tubulin binds to and modifies the structure of lipid membranes even at nanomolar concentrations. Considering that there is up to 10 pM of free dimeric tubulin in cells, our results suggest a new broad regulatory role of dimeric tubulin in vivo.

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Membrane Interactions with NA-CATH
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The “catastrophic threat” of antibiotic resistance has prompted research into biological methods of combating bacterial infection. One such pervasive strategy employs cationic antimicrobial peptides, CAMPs. These peptides use their biological methods of combating bacterial infection. One such pervasive strategy employs cationic antimicrobial peptides, CAMPs. These peptides use their...