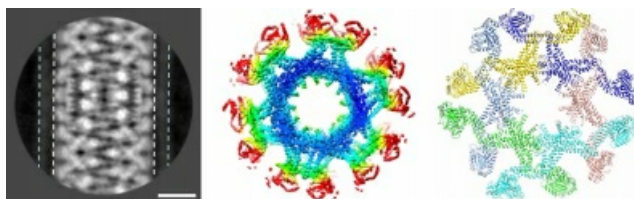


*CryoEM structure of dynamin-like MxB in assembly*Peijun Zhang<sup>1</sup>, Frances Alvarez<sup>2</sup>, Shaoda He<sup>3</sup>, Juan Perilla<sup>4</sup>, Sooin Jang<sup>5</sup>, Alan Engelman<sup>5</sup>, Sjors Scheres<sup>3</sup>

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Human dynamin-like, interferon-induced myxovirus resistance 2 (Mx2/MxB) is a potent inhibitor of HIV-1 infection and a potential agent for the treatment of HIV/AIDS. MxB directly interacts with the HIV-1 capsid and blocks nuclear import of pre-integration complexes and subsequent chromosomal integration of the viral cDNA. Anti-HIV-1 activity and capsid-binding require the N-terminal domain of MxB and protein oligomerization, yet each of these has eluded structural determination due to difficulties in protein preparation. We purified a GTPase active MBP fusion of the full-length wild-type MxB from mammalian cells. The full-length MxB purifies as discrete oligomers and further self-assembles into helical arrays in physiological salt. Intriguingly, GTP, but not GDP, binding to MxB results in array disassembly, while subsequent GTP hydrolysis allows its re-formation. Using cryoEM, we determined the MxB assembly structure at 4.6 Å resolution, revealing novel oligomerization and higher-order assembly interfaces that were absent or are distinct from the crystal structure of MxB that lacked the N-terminal domain and harbored interface mutations. The structure suggests that salt bridges mediate MxB higher-order assembly, which is disrupted by GTP-induced conformational changes. More importantly, mutational analysis combined with viral infectivity assays revealed that MxB oligomers, not the dimer or higher-order assemblies, are in fact the active species against HIV-1 infection. The near-atomic wild-type MxB structure provides a vital framework for re-evaluating conflicting results regarding the effects of MxB oligomerization and GTPase activity on its anti-HIV-1 activity. Moreover, this first high-resolution assembly structure among the superfamily of dynamin-like large GTPases allows us to propose a new GTP-dependent assembly/disassembly model, distinct from current models.



**Keywords:** [cryoEM](#), [MxB](#), [HIV-1](#)