Grafton High School SMART Team
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"Buzz Off" Zika

PDB File: 5KQR

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Zika virus, or ZIKV, a mosquito-borne pathogen, is a current public health concern due to its link to microcephaly and Guillain-Barré syndrome. A flavivirus, ZIKV contains an RNA genome translated using the host cell's protein synthesis machinery. The 5' end of the viral RNA possesses a "cap" of methylated bases that protect it from being destroyed by the host's immune system. This cap is produced by a virally-encoded methyltransferase enzyme, the NS5 methyltransferase (MTase). Since the 5'-RNA cap is required for viral reproduction, inactivating the NS5 MTase with a small molecule inhibitor should be a viable treatment for ZIKV infections. The NS5 MTase transfers CH_3 groups from the ubiquitous methyl donor molecule S-adenosylmethionine (SAM) to specific positions on bases at the 5' end of the viral RNA. Based on the binding mode of SAM observed in a crystal structure (5KQR), an analog of SAM was developed that could inhibit the enzymatic activity of the MTase. SAM binds in a pocket composed of Ser56, Arg84, Trp87, Thr104, Lys105, His110, Glu111, Asp131, Val132, Phe133, Asp146, and Ile147. The Grafton SMART (Students Modeling A Research Topic) Team has modeled the NS5 MTase with either SAM or the hypothetical inhibitor MO2 bound using 3D printing technology. Models with such compounds bound to the enzyme provide information that might help increase the potency of potential inhibitors and improve their selectivity for the ZIKV MTase.

Specifications:
Helices: mediumturquoise
Sheets: mediumpurple
7-MeGPP: fuchsia
SAM/MO2: lime
H-Bonds: honeydew
Struts: lavenderblush