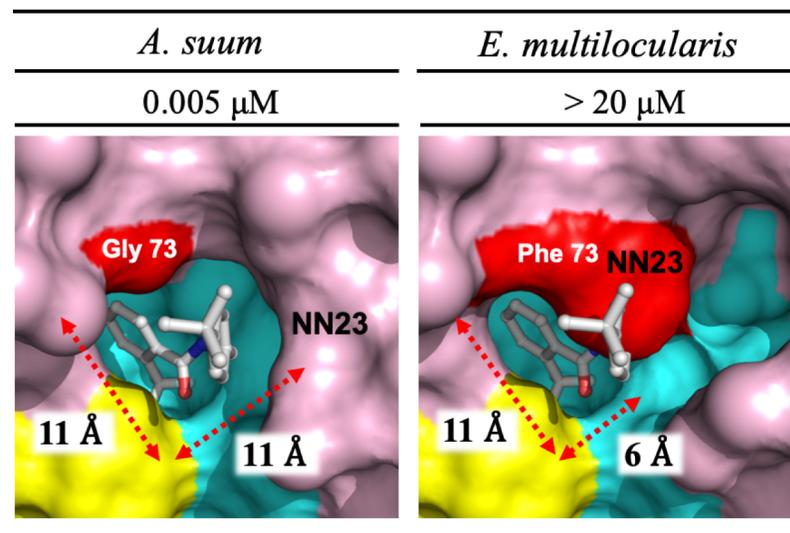
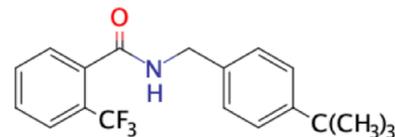


Supplementary Figure 1. Chemical structure of ascofuranone (AF). The benzene, linker, and terminal groups are shown. The asterisk represents the chiral carbon (adapted from Miyazaki *et al.* [1])

NN23 (Flutolanil derivative)



Supplementary Figure 2. Model structure of NN23 bound to the quinone binding site of complex II from *E. multilocularis* based on the reported co-crystal structure (PDB 4YSX) of *A. suum* complex II with NN23. Protein subunits are colored as follows: Ip (cyan), CybL (purple), and CybS (yellow). The dimensions of the entrance to the quinone binding site of *A. suum* and *E. multilocularis* complex II are shown as in Figure 4. As rendered in ball-and-stick, NN23 binds tightly to *A. suum* complex II ($\text{IC}_{50} = 0.005 \mu\text{M}$), but it did not inhibit *E. multilocularis* complex II ($\text{IC}_{50} > 20 \mu\text{M}$) due to the steric hindrance between Phe73C and the tert-butylbenzene group of NN23.

References

- [1] Miyazaki Y, Inaoka DK, Shiba T, Saimoto H, Sakura T, Amalia E, Kido Y, Sakai C, Nakamura M, Anthony L Moore, Harada S, Kita K. 2018. Selective Cytotoxicity of Dihydroorotate Dehydrogenase Inhibitors to Human Cancer Cells Under Hypoxia and Nutrient-Deprived Conditions. *Front Pharmacol* 9:997.