

Journal Club Summary:

A new class of synthetic retinoid antibiotics effective against bacterial persisters.

By Kim et al., Nature 2018

The present work reports the identification, based on a high-throughput screen *in vivo*, of retinoid derivatives with potent gram-positive antimicrobial activity including in antibiotic tolerant cells. The mechanism of antimicrobial action is attributed to membrane destabilization. Despite their antimicrobial activity, lead compounds are fraught with toxicity. An effort to modify the lead compounds to develop a new compound that has an improved toxicity/activity profile is describe. While the work is very impressive, the experiments are not homogenously presented (toxicity read out at 1 hour, lethality assays at 4 hours). The proposed mechanism of action is questionable as some of the leads do not recapitulate all of the phenotype. Most significant, no data *in vitro* is shown regarding the lethality of analog 2. Still, presenting a novel class of broadly acting gram positive bacteria in a translational fashion is timely and welcome.