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IN BRIEF

PARASITE BIOLOGY

Punching through vacuolar membranes

Some apicomplexan parasites, including *Toxoplasma gondii* and *Plasmodium falciparum*, replicate within parasitophorous vacuoles (PVs) after invading the host cell. Amino acids and other metabolites that are essential for parasite growth are delivered to the PV by transport through its membrane, which is made selectively permeable to small molecules by an unknown mechanism. Gold *et al.* now identify a novel *T. gondii* protein, GRA17, that localizes to the PV, and they propose that it forms a metabolite-permissive pore. Parasites lacking GRA17 were defective in small molecule transport across the PV membrane and were impaired in growth and virulence. Notably, these phenotypes could be rescued by the *P. falciparum* protein EXP-2, which is a component of the PTEX (*Plasmodium* translocon of exported proteins) complex. The complementarity between GRA17 and EXP-2 suggests a new function for EXP-2 in the transport of small molecules across the PV membrane.

ORIGINAL RESEARCH PAPER Gold, D. A. *et al.* The *Toxoplasma* dense granule proteins GRA17 and GRA23 mediate the movement of small molecules between the host and the parasitophorous vacuole. *Cell Host Microbe* **17**, 642–652 (2015)

ANTIMICROBIALS

Fine-tuned antifungals

Resistance to the antifungal drug Amphotericin B (AmB) has not evolved but it is extremely toxic to humans. AmB extracts the fungal sterol ergosterol from fungal membranes and its toxicity probably results from cross-reactivity with human cholesterol. Davis *et al.* designed a new class of non-toxic amphotericins that are readily synthesized from AmB. Crucially, the disruption of a salt bridge in AmB produces an alternative conformer that binds to ergosterol but not cholesterol. *In vitro* tests showed potency against several fungal pathogens but little or no human toxicity. In a mouse model of candidiasis, one compound, AmBMU, was more potent than AmB, with no observed toxicity. A small number of mutations were identified that conferred resistance to AmBMU but these rendered the pathogen avirulent, suggesting that the use of non-toxic amphotericins is unlikely to select for drug resistance.

ORIGINAL RESEARCH PAPER Davis, S. A. *et al.* Nontoxic antimicrobials that evade drug resistance. *Nat. Chem. Biol.* http://dx.doi.org/10.1038/nchembio.1821 (2015)

MICROBIOME

A gut instinct for recovery

Childhood diarrhoea is associated with infection of the gut by pathogens such as *Vibrio cholerae* and enterotoxigenic *Escherichia coli* (ETEC), but how the gut microbiota recovers post infection is incompletely understood. David *et al.* analysed the microbiome of rectal samples from 13 patients with cholera and 18 patients with ETEC at early, mid and late stages during recovery. Recovery to a normal microbiome occurred only at the late stage, 30 days after infection, but distinct groups of bacteria were reproducibly present at the early and mid stages. Taxonomic and functional data supported a succession model in which infection-induced diarrhoea depletes the gut microbiota, resulting in elevated oxygen and carbohydrate levels in the gut; facultative anaerobes that reach the gut by food ingestion or by migration then colonize the gut; aerobic respiration by these bacteria lowers the oxygen levels in the gut; as oxygen levels fall, obligate anaerobes recolonize the gut and alter the carbohydrate composition to favour 'healthy' commensals and promote recovery.

ORIGINAL RESEARCH PAPER David, L. A. *et al.* Gut microbial succession follows acute secretory diarrhea in humans. *mBio* **6**, e00381-15 (2015)