Small Molecule Inhibitors of Multicellular Development in Social Amoeba

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What are the small molecules that orchestrate, or interfere with, multicellular associations in eukaryotes?

The social amoeba *Dictyostelium discoideum* represents one of the earliest branches of the common ancestor of all eukaryotes. It is thus an ideal model organism to study general eukaryotic communication and cellular mechanisms. Since it can exist both in a single-cell and a multicellular state, *D. discoideum* serves as a paradigm in understanding the onset of multicellularity. Differentiation and multicellularity in this protist have evolved in a setting where they are surrounded by food sources (e.g. bacteria), as well as predators. Only in the light of this ecologically relevant context, a deep understanding of the fundamental molecular communication and signaling processes can be gained. Understanding how small molecules selectively interfere with the early eukaryote's association machinery will provide us with insight for deciphering and modulating basic cellular mechanisms.

The social amoeba *D. discoideum* typically preys on bacteria, yet it can also serve as a food source for the related dictyostelid *D. caveatum*. [1] This feature was first described 30 years ago and has since been subject to further investigations. Importantly, *D. caveatum* can only feed on *D. discoideum,* if the latter is present in the single-cell state. Previous studies have shown that *D. caveatum* secretes a factor that effectively freezes *D. discoideum* in the single cell state, by inhibiting formation of the multicellular fruiting body (Fig. 1). While preliminary experiments clearly show that a small diffusible molecule is the responsible morphogenesis inhibitor, its structure, biosynthesis, and mode of action remain elusive.

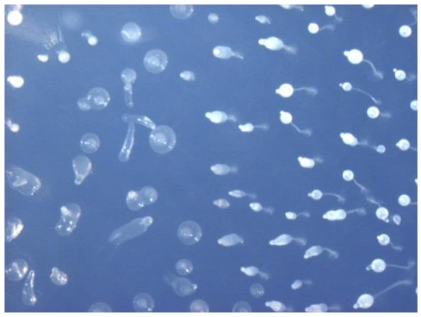

Fig. 1. Different stages *of D. discoideum development.*

While preliminary experiments clearly show that a small diffusible molecule is the responsible morphogenesis inhibitor, its structure, biosynthesis, and mode of action remain elusive. [2] We utilize bio-assay guided fractionation to attempt to isolate and elucidate the structure of the small molecule responsible for the inhibition of multicellular development in *Dictyostelium discoideum*.

References:

[1]. Waddell, D. R., & Vogel, G. (1985). Phagocytic behavior of the predatory slime mold, Dictyostelium caveatum. Cell nibbling. [Research Support, Non-U.S. Gov't]. *Experimental Cell Research, 159*(2), 323-334.

[2]. Nizak, C., Fitzhenry, R. J., & Kessin, R. H. (2007). Exploitation of other social amoebae by Dictyostelium caveatum. [Research Support, Non-U.S. Gov't]. *PLoS One, 2*(2), e212. doi: 10.1371/journal.pone.0000212