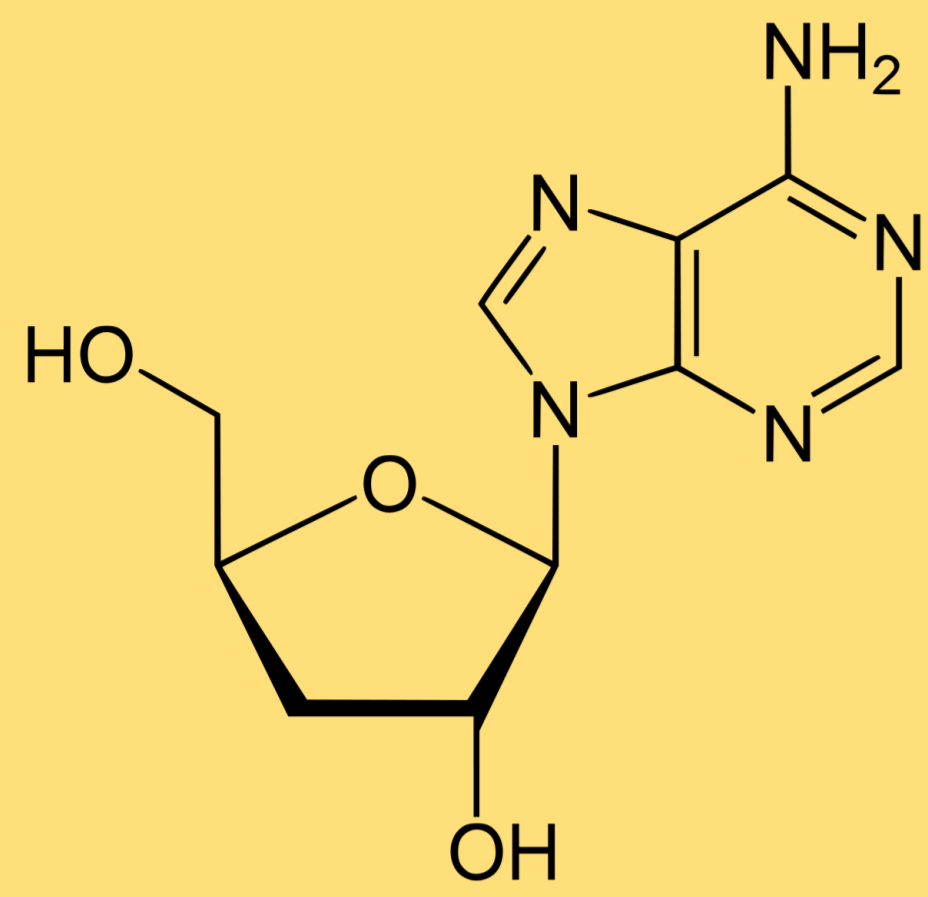


Cordycepin Suppresses the Upregulation of Innate Immune Response Genes in Mouse and *Drosophila melanogaster* Cell Lines



Cordycepin

Cordycepin, or 3'-deoxyadenosine, is a metabolite secreted by the fungal entomopathogen *Cordyceps militaris* and closely related fungal species [1].

It is known for anti-inflammatory effects mediated by the degradation of mRNA poly(A) tails, as well as other gene expression inhibitory roles including effects on mTOR and AMPK signalling, dephosphorylation of eukaryotic translation initiation factor 4E-binding protein [2], and inhibition of cell attachment at higher doses [2]. These have possible applications in medicine for example in treatment of arthritis [3].

Rationale

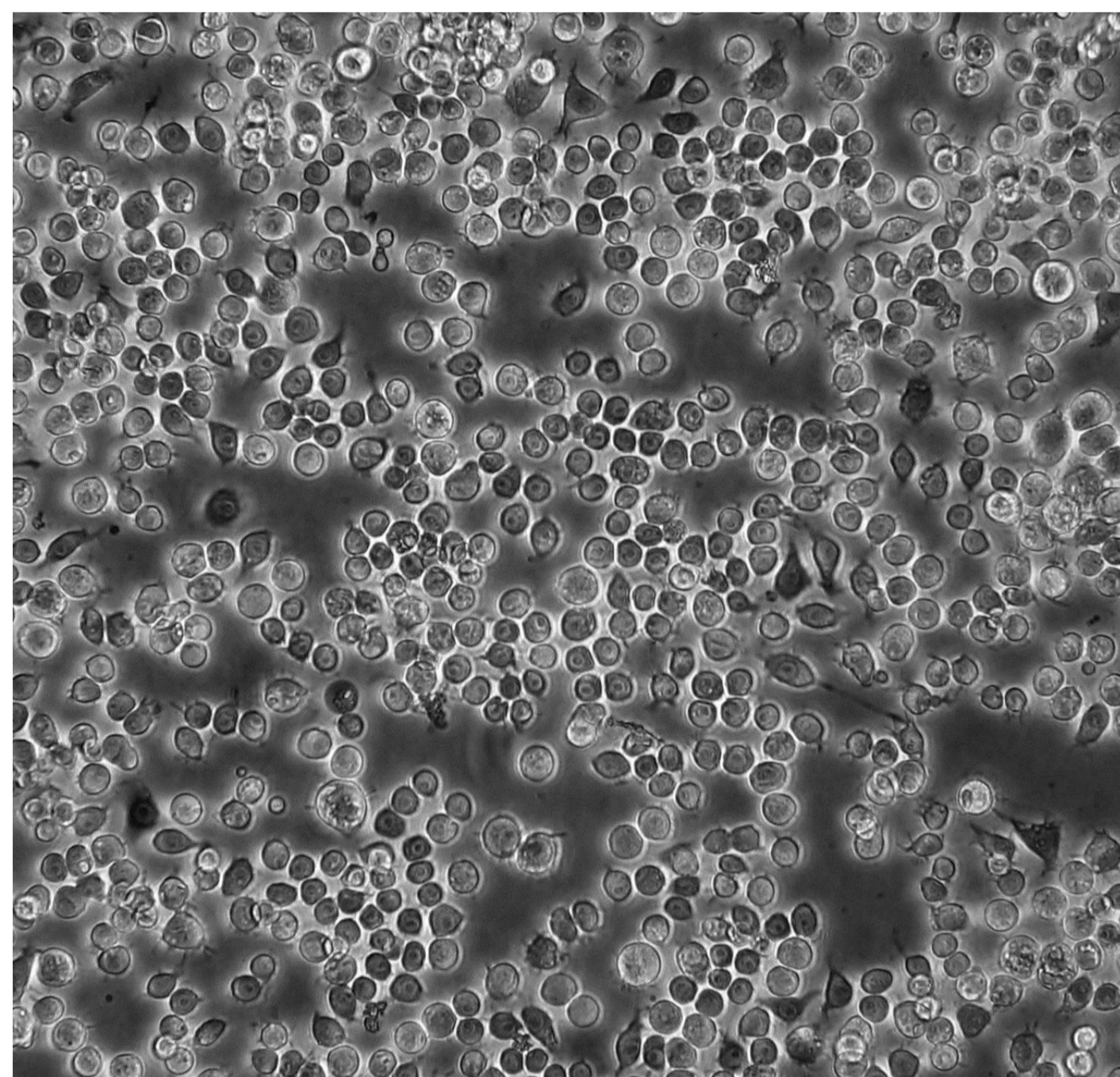
The metabolic pathways, mechanisms, and phenotypic effects concerning cordycepin and other small molecules within *Cordyceps*-host systems is of considerable interest due to potential future development of control strategies for crop pest insects.

The suppression of genes of interest by cordycepin was tested here *in vitro* using animal cell cultures and quantitative PCR.

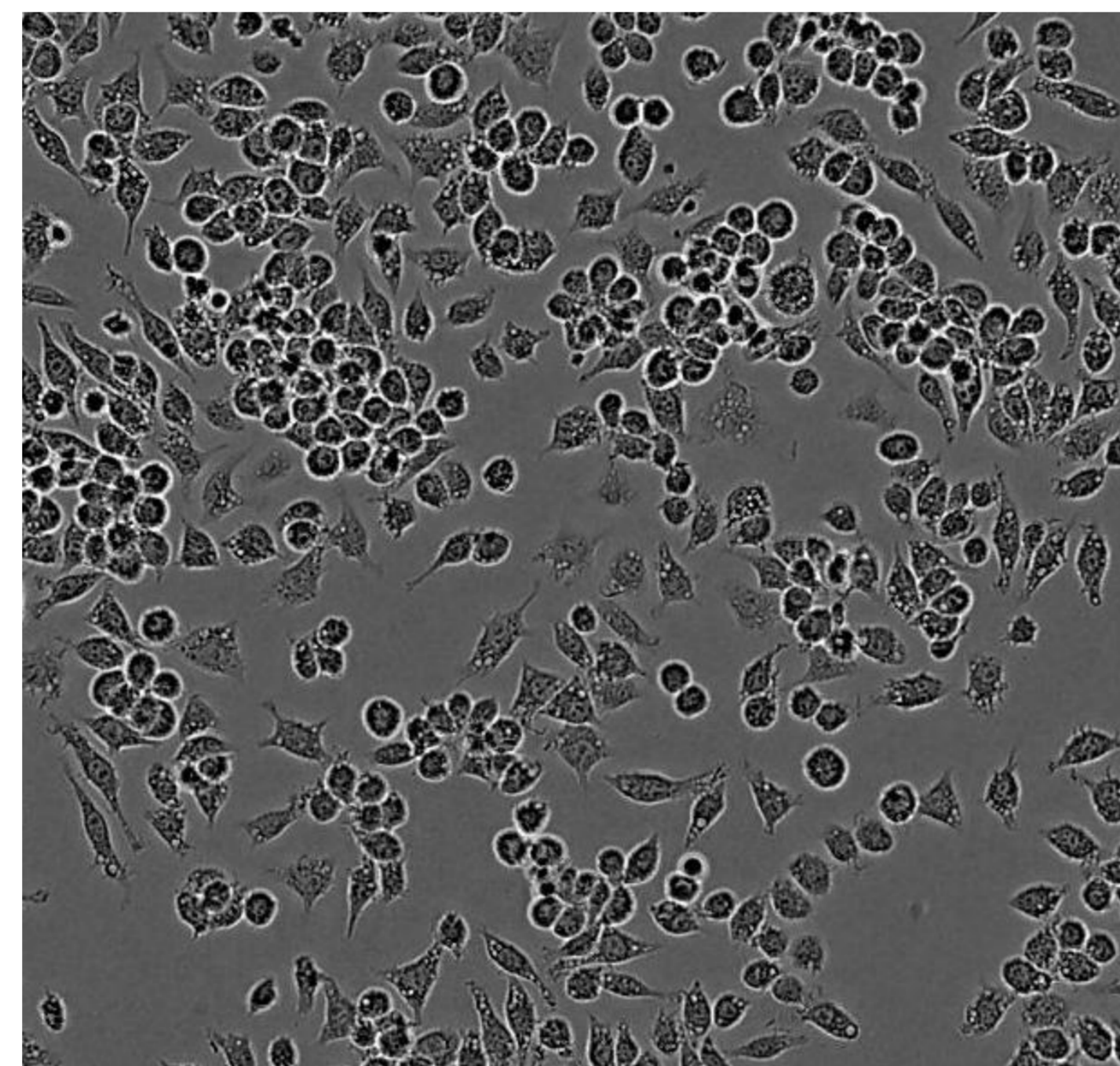


Cordyceps militaris

In Vitro Cell Lines Tested



Drosophila melanogaster
Schneider 2 (S2) Cells

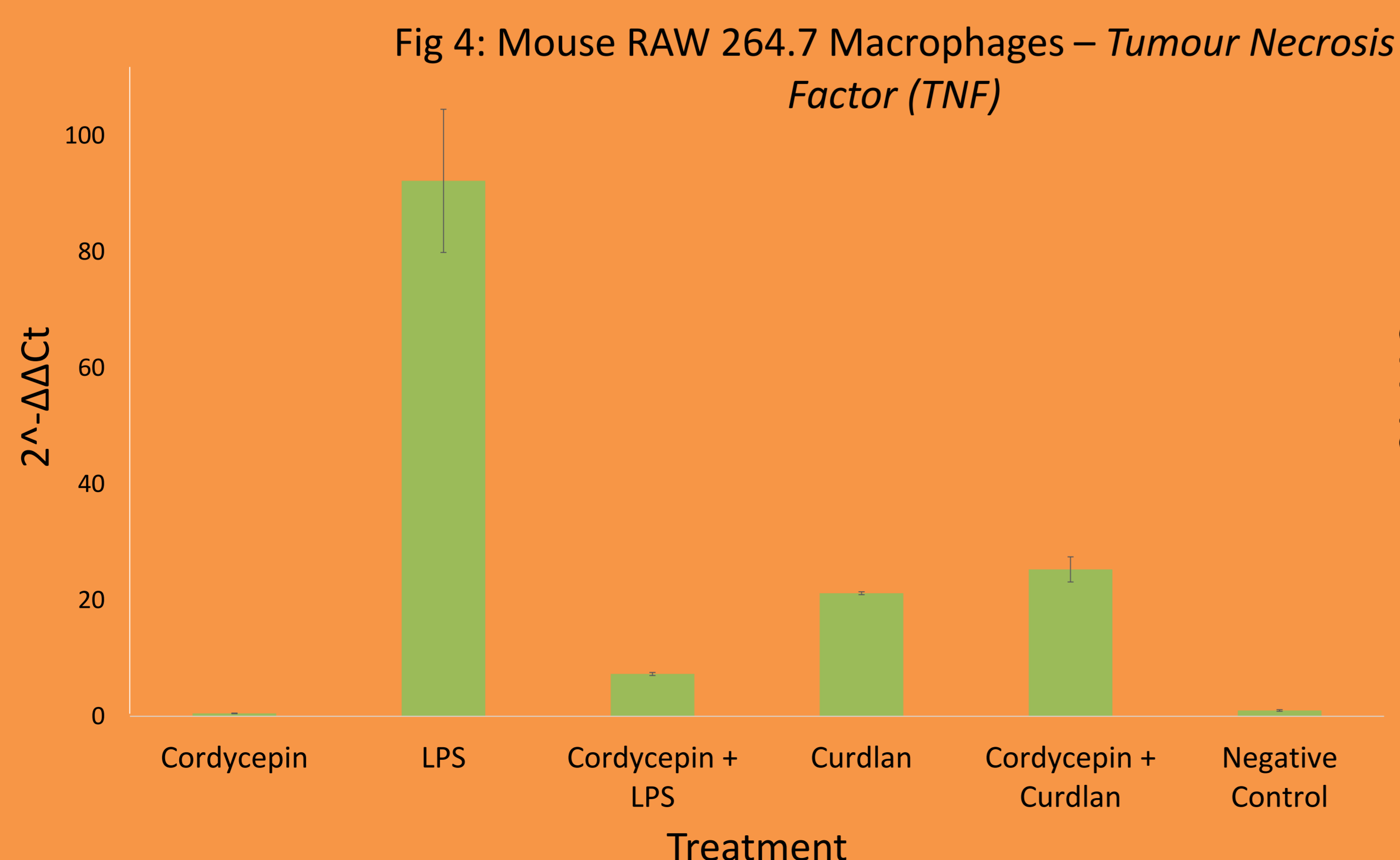


Mouse RAW 264.7
Macrophages

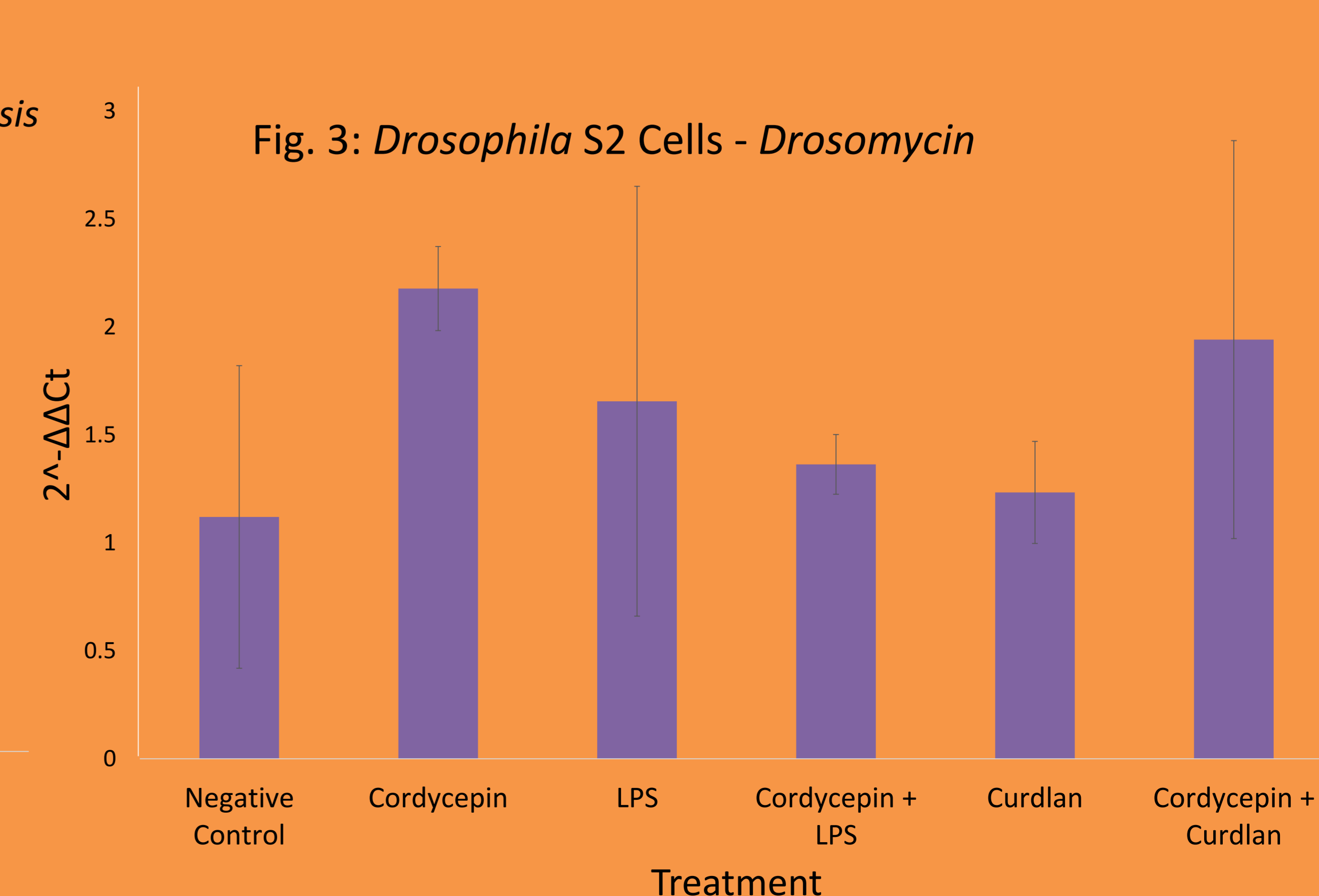
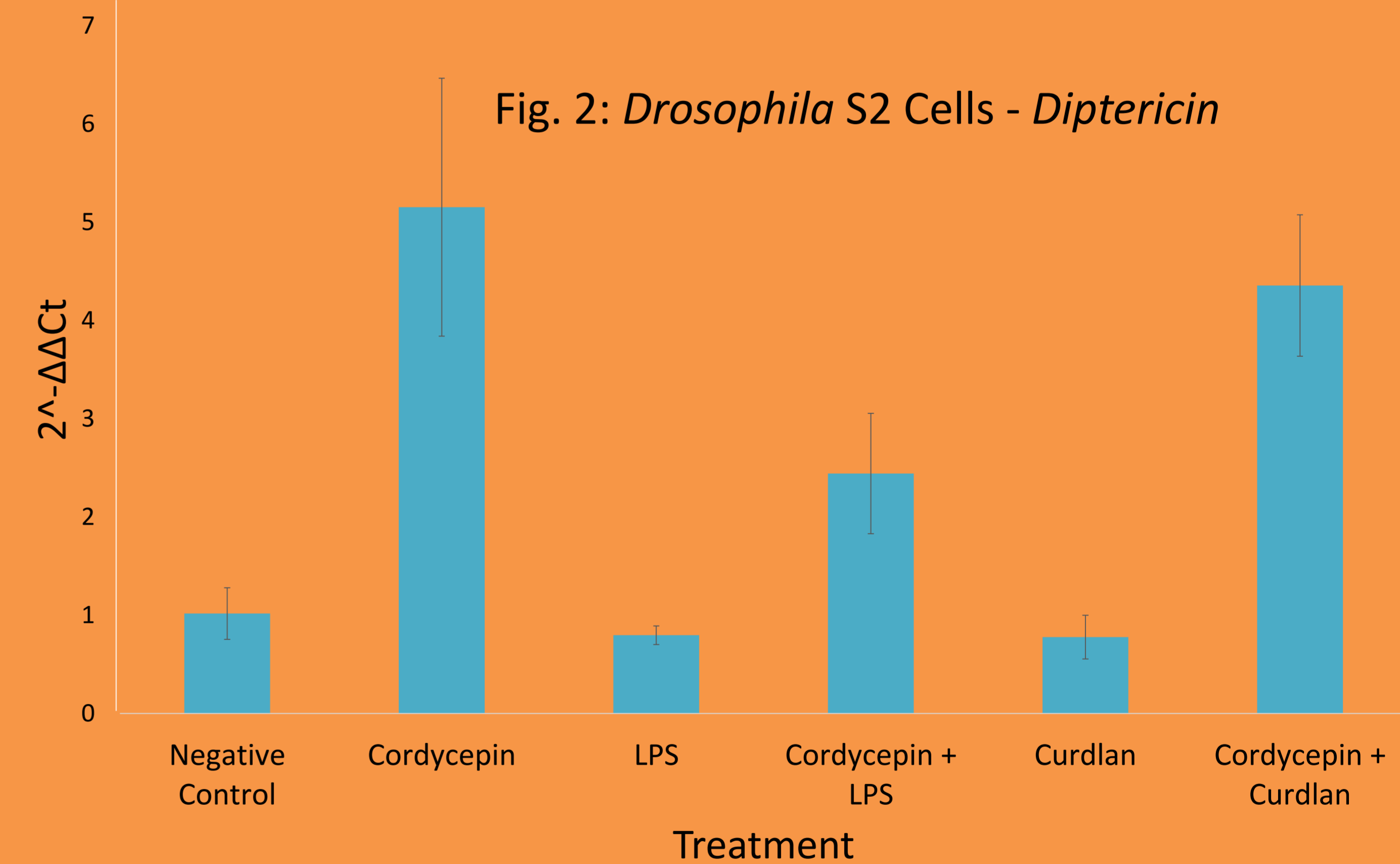
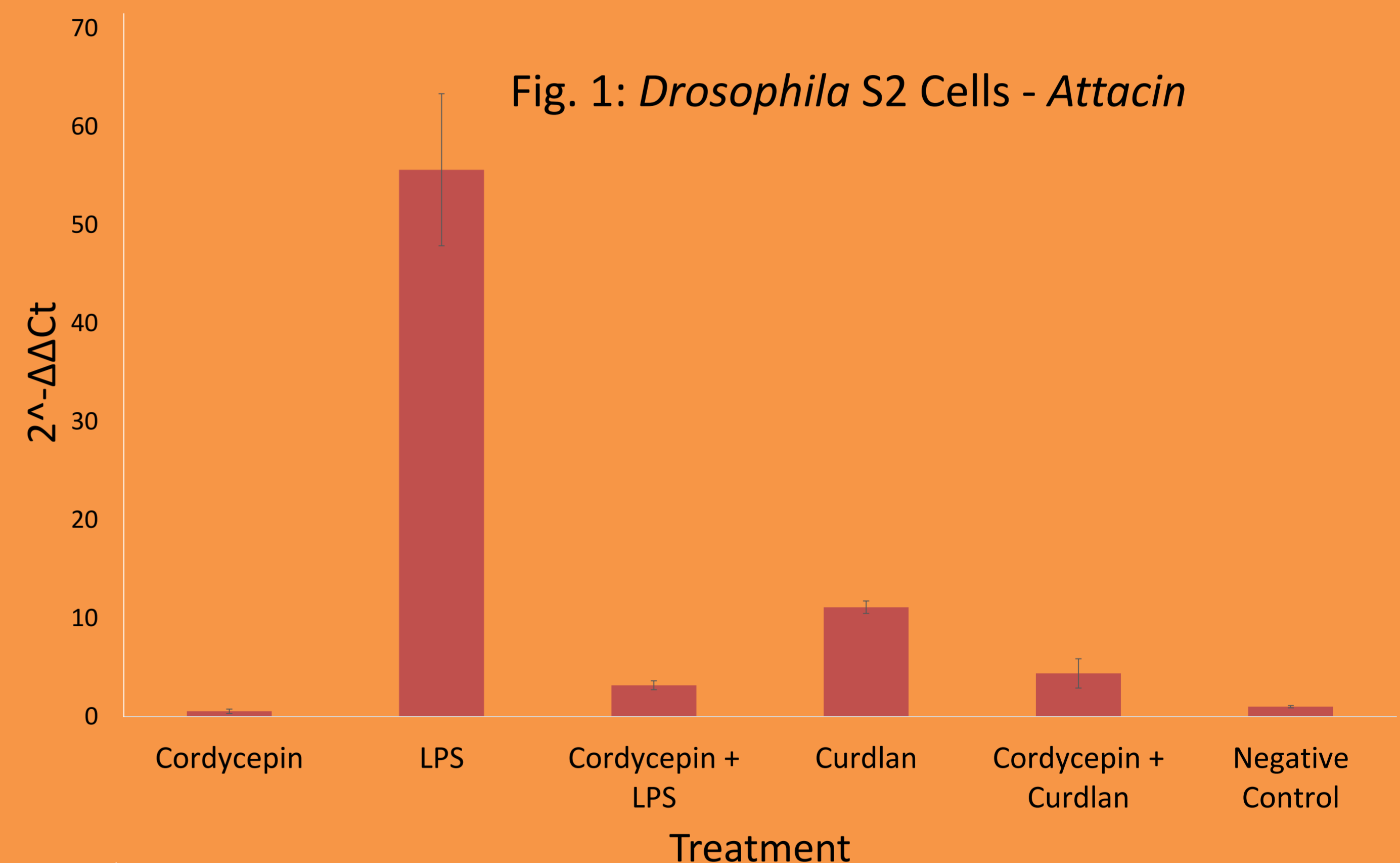
Methods Near confluent (~70%) cells in culture were stimulated with bacterial lipopolysaccharide (LPS) and curdlan [4,5] serums (20µg/ml and 1µg/ml for S2 and RAW cells respectively). Some treatment groups were pre-treated with cordycepin (100µM and 20µM), and expression of genes of interest [4] were compared following qPCR.

In S2 cells, *Attacin* (Fig. 1) and *Metchnikowin* were upregulated by LPS and curdlan treatment; these responses were suppressed by cordycepin. Similar effects were observed for RAW cell expression of *TNF*. *Attacin* and *TNF* can therefore be regarded as suitable genes of interest for model *in vitro* systems of cordycepin suppression of immune response in *Drosophila melanogaster*

and mice respectively. *Diptericin* (Fig. 2) and *Drosomycin* (Fig. 3) both showed minimal levels of expression in S2 cells.



Results



References:

1. Cunningham *et al.* (1950) *Nature*; 2. Wong *et al.* (2010) *J. Biol. Chem.*; 3. Noh *et al.* (2008) *Rheumatology*; 4. Jin *et al.* (2007) *Mol. & Cells*; 5. Virca *et al.* (1989) *J. Biol. Chem.*