

73. From Genomes to Metabolomes: Interspecies Interaction in the Archaeal System *Ignicoccus-Nanoarchaeum* and in other Nanoarchaeota

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Project Goals: Archaea harbor specific genomic, biochemical and membrane level adaptations that enable them to thrive under chronic energy stress. Nanoarchaeota are hyperthermophilic archaea dependent on direct interaction with other archaea and appear to have pushed that limit even further by becoming nutritional and energetic parasites. Two such systems have been characterized so far, one in our laboratory (Podar et al, 2013). This project integrates comparative genomics with molecular microbiology, proteomics, transcriptomics and metabolomics to understand the mechanisms and evolutionary history of such archaeal relationships. Principles and approaches resulting from this work will also be applied to studying more complex microbial consortia and syntrophic associations.

The marine crenarchaeon *Ignicoccus hospitalis* supports the propagation on its surface of the nanoarchaeote *Nanoarchaeum equitans*. We used concerted proteomic and transcriptomic analyses to probe into the functional genomic response of *I. hospitalis* as *N. equitans* multiplies on its surface. The expression of over 97% of the genes was detected at mRNA level and over 80% of the predicted proteins were identified and their relative abundance measured by proteomics. These indicate that little if any genomic information is silenced during the growth of *I. hospitalis* in the laboratory. The primary response to *N. equitans* was at the membrane level, with increases in relative abundance of most protein complexes involved in energy generation as well as that of several transporters and proteins involved in cellular membrane stabilization. Similar up-regulation was observed for genes and proteins involved in key metabolic steps controlling nitrogen and carbon metabolism, although the overall biosynthetic pathways were marginally impacted. Proliferation of *N. equitans* resulted, however, in selective down regulation of transcription factors, replication and cell cycle control genes as *I. hospitalis* shifted its physiology from its own cellular growth to supporting that of its ectosymbiont/parasite (Giannone et al, 2014). Metabolomic analysis (MS and NMR) has identified specific small molecules and metabolic profiles associated with *N. equitans* proliferation. The majority of metabolites were observed to be present at lower concentrations in the co-culture, suggesting that there is a higher energy demand when *N. equitans* is present. Additionally, trehalose, an osmolite that protects cells from osmotic stress, was readily observed in the co-culture. This compound may mitigate changes in cell volume and membrane-level stress likely to occur during association. Correlations with the proteomic data aim at developing an integrated molecular model for the interspecies interaction.

The interaction between the two organisms is specific. Co-cultivation with other related species of *Ignicoccus* revealed that *N. equitans* can attach to, but is not able to actively divide, on their surface. This suggests that specific mechanisms of interaction, likely involving membrane proteins have evolved to a high degree of specificity. Comparative genomics, cellular and membrane biochemistry, and are used to study interspecies interaction and metabolic transfers.

Comparisons with a Nanoarchaeota system we isolated from a terrestrial thermal system from Yellowstone are used to understand the broader mechanisms of interactions between symbiotic/parasitic archaea and their hosts.

References

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2. Giannone RJ, Wurch LL, Heimerl T, Martin S, Yang Z, Huber H, Rachel R, Hettich RL, Podar M. (2014) Life on the edge: Functional genomic response of *Ignicoccus hospitalis* to the proliferation of *Nanoarchaeum equitans*. Submitted.

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