Goldschmidt 2025 Abstract
https://doi.org/10.7185/gold2025.29622

Non-enzymatic methylation of tetrahydrofolic acid: implications for the emergence of autotrophic metabolism

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The reaction between CO_2 and H_2 is the center of the most ancient carbon metabolism, the reductive acetyl-CoA or Wood-Ljungdahl pathway (WLP). Previous research has shown parallels between hydrothermal conditions, mineral-assisted CO_2 fixation with H_2 and the enzymatically catalyzed steps of the WLP hinting towards the abiotic beginnings of metabolism [1]. Organic cofactors, helper molecules, used by the enzymes of the WLP, could help bridge the gap between mineral and enzymatic catalysis. Here, we show that a central methyl-carrier cofactor, tetrahydrofolate (H_4F), can be methylated non-enzymatically starting from CO_2 and H_2 under conditions found in naturally occurring rock-water-interaction systems (6.5 mM H_2, 510 mM CO_2, FeNi mineral powder, 60 °C, pH 6). These results are in line with previous work conducted on non-enzymatic reactions on H_4F [2], and mark the first complete non-enzymatic methyl-branch of the WLP resulting in a biochemical methyl-group carrier. This is in line with former phylogenetic studies claiming that the enzymes of the methyl-branch constitute a later addition to the WLP, with acetyl-CoA synthase directly using methyl-groups provided by the environment [3]. This study opens up a new direction of research, showing how the geochemical environment of an early Earth could have taken over concrete enzymatic steps of early metabolism. Such investigations complement phylogenetic efforts trying to determine the order of emergence of WLP enzymes.

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