Microbes in terrestrial environments regulate many vitally important processes, including mediating greenhouse gas fluxes and contaminant remediation. In spite of their critical role, little is known about complex interactions among microbes, minerals, migrating fluids and dissolved constituents that emerge in heterogeneous terrestrial environments across a great range of scales. The new, Department of Energy sponsored ‘Sustainable Systems 2.0’ project aims to develop a predictive understanding of how the subsurface microbiome affects biogeochemical watershed functioning, how watershed-scale processes affect microbial functioning, and how these interactions co-evolve with climate and land-use changes. The initial project investigations are being carried out at a Colorado River floodplain located in Rifle CO. This presentation will describe recent project advances: metagenomic analysis revealing the extraordinary genomic diversity of aquifer microbiomes and their roles in terrestrial system biogeochemical cycling; soil, vadose zone and groundwater biogeochemical monitoring revealing high spatiotemporal variability of DOC in response to hydrological pulses; approaches for quantifying organic-mineral associations; field redox manipulation responses; and progress in developing a genome-enabled watershed simulation capability.