Predicting the thermomechanical behavior of nuclear fuel as it evolves during operation in a reactor is a highly complex problem. Not only are the fuel elements (typically UO₂ pellets cladded by a Zr-based alloy tube) subjected to radiation damage, but the actually fuel composition itself varies as the U atoms are fissioned. The behavior of the resulting fission products is important, as is their effect on the properties (e.g. thermal conductivity) that govern the performance of the fuel. Despite this complexity, mathematical models for the simulation of fuel performance have been used very successfully for nearly 50 years. For light water reactor (LWR) fuel, so-called fuel performance codes have benefitted from considerable experimental data from which a number of thermomechanical models that describe the key phenomena of interest. The large number of nuclear reactors currently operating safely across the globe confirms that these codes are adequate within the empirical parameter space to which they were developed. However, there are several compelling reasons to pursue modern multiscale modeling for nuclear materials, including (but not limited to): (1) improved understanding of fuel performance phenomena that can lead to improved safety margins, (2) the capability to predict fuels and clad performance for compositions other than those for which irradiation performance data already exists, (e.g. UO₂ and Zircaloy), and (3) extension reactor conditions or designs for which little experimental data exists and for experiments that are particularly demanding (e.g. transient conditions). In this presentation, several examples of how atomistic and mesoscale simulations can support engineering scale fuel performance codes. These examples will highlight new discoveries in old materials (e.g. explanation of the anomalously low thermal conductivity of UO₂) as well predictions of fuel behavior for new proposed fuel compounds for which no experimental data exists (e.g. fission gas diffusion in accident tolerant fuel compounds).