Darwin had two fundamental insights that changed the field of biology and more generally the way we understand the world we live in. The first was that all organisms have descended with modification from common ancestors. The second was that the major agent of modification is natural selection acting on variation between individuals. However, Darwin lacked a correct understanding of inheritance, and thus could not link his two insights into a logically complete theory. With the subsequent discoveries of Mendelian genetics and DNA as the unit of inheritance, evolutionary biologists were finally able to understand how variation could be passed from one generation to the next. The development of molecular biology and high throughput genomic sequencing is now allowing us to identify genetic variation at finer and finer scales. In parallel, a rich history of field experiments over the last 150 years have amassed thousands of examples of natural selection acting on phenotypic traits. An exciting development in recent years is the combination of these two approaches to document the molecular consequences of natural selection in action, thereby fully connecting Darwin's two insights. Here, I will describe some examples of my work with threespine stickleback fish and deer mice that use experiments to directly estimate how selection impacts the genome as populations adapt to new environments. These studies are helping us to understand the targets and mechanisms of evolution by natural selection, and collectively show how Darwinian principles now play a greater role in biology than ever before.