Cell biological studies are limited by available technologies. For much of history, genomic and/or proteomic techniques were either completely unavailable or accessible by only a few experts, and microscopy techniques could only image one cell at a time. Today, modern microscopes have long surpassed their predecessors, capable of imaging tens to thousands of individual cells at once. In addition, many research centers now also have genomic and/or proteomic cores capable of analyzing large data sets. We and others are focusing these readily available technologies on re-examining a classic question: how does force-generating machinery assemble and function within a cell? Our lab focuses on the first molecular motor that was discovered, myosin II. The classical function of myosin II is to generate "contractile" forces, generated by myosin heavy chains pulling on actin filaments. However, it is now known that myosin II-based contraction drives a plethora of other important cellular processes, including cell division, nuclear positioning, membrane bleb formation and retraction, 3D cell migration, tissue morphogenesis, mitochondrial fission, focal adhesion maturation, stem cell differentiation, retrograde flow of actin filaments, cell shape changes and the metastasis of solid tumors. Not surprisingly, there are multiple myosin II paralogs (i.e., heavy chains produced by different genes) that are used to accomplish these tasks. I will discuss our recent efforts investigating two widely expressed myosin II paralogs, myosin IIA and myosin IIB. These paralogs are often referred to as "non-muscle", but are expressed in both muscle and non-muscle cell types. Notably, our data suggest that myosin IIA and myosin IIB work in tandem to tune contractility within a cell. In our hands, this is particularly clear during mitosis and cytokinesis in non-muscle cells. Our data also suggest that IIA/IIB are vital for forming a muscle sarcomere, the contractile unit within cardiomyocytes which drives heart muscle contraction. These findings have prompted us to take a closer look at similarities and differences between the assembly of myosin II-based contractile systems in muscle versus non-muscle cells. For this work, we created an assay using human cardiomyocytes to monitor sarcomere assembly, finding that a population of muscle stress fibers (which appear similar to actin arcs in non-muscle cells) are essential sarcomere precursors. We are now using this assay to explore the mechanisms underlying stress fiber assembly, as well as the transition of these stress fibers into the sarcomere-containing "myofibrils" that drive the heartbeat.