Humans relate in a very dynamic way with their microbial environment. Sudden modifications to this environment have resulted in a large death toll in human populations through the ages accompanied by a struggled to adapt and survive, biologically and societally. Fresh to memory is the recent scare of a swine flu pandemic. Computational modeling has impacted our understanding of Influenza A virus-human relationship and the impact of containment strategies at the host and societal levels. Yet, predicting the emergence of strains of significant pandemic potential is still at the embryonic stage. Multiscale computational models, improving local and global surveillance data, and high throughput gene sequencing of evolving viral genomes yield a set of tools that has potential to address this difficult problem effectively. We will review efforts by our transdiciplinary team to integrate such tools in the context of Influenza A virus, and guide the development of effective containment measures.