We investigated the use of deep neural networks to analyze complex morphological phenotypes and predict the activation of signaling networks. Drug resistance can lead to changes in cell morphology, and we hypothesized that Deep Learning could be used to elucidate the relationship between cell shape and signaling. To test this hypothesis we performed a large high content screen on drug sensitive and drug resistance cancer cells, and analyzed the shape of these cells using a deep neural network. We identified a continuous 27-dimension space describing the observed cell morphologies from which we were able to predict drug resistance with an accuracy of 74%. In addition, analyzing changes in cell morphology identified signaling networks that, when perturbed, caused the death of drug resistant cells. However genes identified by morphological analysis were not enriched for anti-proliferative or highly differentially expressed genes. These findings suggest that complex morphologies can decode states of signaling networks seemingly unrelated to cell shape, and that analysis of this information can unravel cellular mechanisms hidden to conventional measurements.