Electron microscopy (EM) is the characterization method of choice to observe the atomic-scale and microstructural local features within materials that play a critical role in material performance. Current EM capabilities include a wide variety of imaging modalities to probe a material’s local structure and chemistry. Furthermore, recent advances in fast electron detection enable imaging at nearly 100 kHz rates. Directly incorporating these EM methods for structural validation into high throughput materials prediction, design and synthesis routines would profoundly speed up the materials discovery process. However, a bottleneck exists between image acquisition and the extraction of relevant information that can be used in a materials design feedback loop. While analysis of individual images can easily identify regions of interest and determine whether they contain defects, it is prohibitively time-consuming to manually perform this analysis on large numbers of images. This means that, for example, in a given nanomaterial synthetic optimization process, only a small number of successful end products are studied in detail. Failure cases are typically not characterized, and population heterogeneity statistics are not captured. Therefore, to automatically identify and quantify defects, size and shape statistics, and other key structural features which can dominate a material’s mechanical, electronic, and catalytic properties, a new approach is required. Advances in machine learning and computer vision have made high accuracy automated image interpretation possible. While widely applied in the life sciences, this approach is only recently being applied to atomic resolution TEM images. Here, we present application of machine learning and other high-throughput methods to EM images for nanoparticle identification and microstructural characterization. When combined with existing automatic image acquisition protocols, this approach is a viable option to close the materials design loop and incorporate EM into high-throughput materials design and synthesis.