Resistance Mechanisms to Palbociclib in Hormone Positive Metastatic Breast Cancer Joshua Donaldson, MD, PhD Senior Medical Oncology Fellow Johns Hopkins University

Women with metastatic hormone sensitive breast cancer are treated with a variety of hormone therapies, but their cancer will inevitably become resistant. CDK inhibitors, such as palbociclib, have recently been approved for patients who stop responding to hormone therapy. Unfortunately, even though palbociclib generally controls the cancer longer than hormone therapy alone, most women will experience recurrence or progression within a few months. Additionally, some tumors demonstrate no response at all to palbociclib. Thus far, efforts to identify nonresponders have been unsuccessful, suggesting that there may be more to learn about the response to palbociclib. This study will 1) look for genes that may be involved in palbociclib resistance or sensitivity in cancer cells and 2) measure the effect of breast cancer gene mutations on palbociclib response. These types of experiments have been successful in other cancer types, including melanoma and lung cancer. Although this research is performed on cancer cells, our group has experience confirming our findings using liquid biopsy techniques from patient samples. Understanding how resistance develops is the first step toward developing more effective treatments.