in normal tissues. Indeed, to date, there is still no MYC inhibitor in the clinic. We previously designed a dominant negative form of MYC called Omomyc and used its conditional transgenic expression to inhibit MYC function both in vitro and in vivo, demonstrating a potent therapeutic impact in various mouse models of cancer, including non-small cell lung cancer (NSCLC), causing only mild, well-tolerated, and reversible side effects. Importantly, we recently showed that the purified Omomyc mini-protein displays unexpected cell-penetrating properties and can be used by direct tissue delivery or systemic administration to target NSCLC harboring different oncogenic mutation profiles, indicating its potential for clinical development for the treatment of NSCLC patients. Clinical trials testing this use are due to begin in 2020.

**IA17**

**Druggable Vulnerabilities in Therapy-Resistant Lung Cancers**

**K.C. Wood** Duke University, Durham, NC/US

Oncogene-targeted therapies often drive therapeutic responses in patients with advanced lung cancers, but frequently these responses eventually give way to acquired resistance. Blocking acquired resistance is a substantial and open-ended challenge whose difficulty is underscored by the fact that resistance within individual patients is often polyclonal in nature, driven by diverse and co-occurring mechanisms. Here, I will discuss two broad approaches we are employing in the search for therapeutic strategies that delay or circumvent resistance evolution. In the first area, we have identified vulnerabilities present in tumors at minimal residual disease states. For example, we have identified a molecular pathway through which targeted therapies such as EGFR, ALK, and BRAF inhibitors trigger double-strand DNA breaks in the cancer cells that comprise the minimal residual disease state. These cells rely upon an ATM-dependent DNA repair process for their survival and are thus hypersensitive to ATM inhibition. As such, combining oncogene-targeted therapies with an ATM inhibitor leads to more penetrant and durable responses to these agents in vivo. In the second area, we have identified vulnerabilities that arise specifically in tumor cells that develop acquired resistance to oncogene-targeted therapies. Importantly, we have identified scenarios in which these “collateral sensitivities” are conserved across heterogeneous resistant clones with distinct resistance mechanisms, implying that targeting these mechanisms may simultaneously eradicate diverse clones. I will describe examples of mechanism-based collateral sensitivities we have uncovered in lung cancers, melanomas, and leukemias, then demonstrate that by targeting these mechanisms in the upfront setting, it is possible to construct combination therapies that select against resistance.

**IA18**

**A New World for Lung Cancer Vaccines: Beyond Picking a Single Antigen for Everyone**

**F.B. Garon** David Geffen School of Medicine at UCLA, Los Angeles, CA/US

Immunotherapy was hypothesized as an effective approach for the treatment of lung cancer for decades. Until the last decade, this enthusiasm was met with the cold reality of clinical trials, showing no benefit in engaging the immune system to fight lung cancer. This string of disappointing clinical trials included several high-profile trials of vaccines targeting a single, specific antigen. While enthusiasm for this approach of vaccines targeting a specific antigen has been reinvigorated in the era of PD-1 and PD-L1 inhibitors (generally in combination with these agents), new approaches to vaccines are also emerging. These new approaches often use patient-specific factors, such as autologous antigen presenting cells or vaccines directed at antigens specific to the patient being treated.