a functional ligand binding domain (Graus-Porta 1997) and Her3 lacks tyrosine kinase activity (Guy 1994), so these receptors must act as heterodimers. Recent evidence shows that other Her family members may also play a role in NSCLC. However their contributions to the disease are less well characterized and studies have often focused on their interactions with EGFR activation (Kuyama et al. 2008, Hirsch 2009, Zhou 2006, Johnson 2006, Ding 2008).

Neuregulin is a ligand for the Her3 and Her4 receptor tyrosine kinases. There are four known members of the neuregulin family, NRG1, NRG2, NRG3, and NRG4 (Falls 2003). The NRG1 transcript undergoes extensive alternative splicing resulting in at least 15 different isoforms. All active isoforms share an EGF-like domain that is necessary and sufficient for activity (Holmes 1992, Yarden 1991). NRG1 autocrine signaling has been shown to regulate lung epithelial cell proliferation (Jinbo 2002) and to play a role in human lung development (Patel 2000) and has been implicated in insensitivity of NSCLC to EGFR inhibitors (Zhou 2006).

The need exists to provide therapeutics effective in treating resistant cancers and patients who have experienced a recurrence of cancer.

SUMMARY

In one aspect, there is provided the use of a neuregulin 1 (NRG1) antagonist and a chemotherapeutic agent in the manufacture of a medicament for increasing time to tumor recurrence in a cancer patient, wherein the chemotherapeutic agent is paclitaxel or cisplatin, or a combination of paclitaxel and cisplatin, and wherein the NRG1 antagonist is an anti-NRG1 antibody, an RNA, or a NRG1 receptor molecule that binds NRG1.

One ~~aspect~~embodiment of the ~~invention~~disclosure provides for a method of increasing time to tumor recurrence in a cancer patient comprising administering to the patient an effective amount of a neuregulin antagonist. In one embodiment, the method further comprises administering a therapeutic agent to the patient. In one embodiment, the therapeutic agent is a chemotherapeutic agent or an antibody. In certain embodiments the chemotherapeutic agent is paclitaxal or cisplatin or a combination of paclitaxal and cisplatin.

In certain embodiments the antibody is an EGFR, HER2, HER3, or HER4 antibody. In certain embodiments, the cancer the patient is suffering from is non-small cell lung cancer, breast cancer, ovarian cancer, head and neck cancer, cervical cancer, bladder cancer, oesophageal cancer, prostate cancer, or colorectal cancer.

In one embodiment, the increase in time to tumor recurrence is at least 1.25 fold greater than the time to recurrence in the absence of the neuregulin antagonist. In one embodiment, the increase in time to tumor recurrence is at least 1.50 fold greater than the time to recurrence in the absence of the neuregulin antagonist.

In certain embodiments, the neuregulin antagonist is an antibody, a small molecule, an immunoadhesin, or an RNA. In one embodiment, the neuregulin antagonist is a NRG1 antagonist. In one embodiment, the NRG antagonist is an anti-NRG1 antibody.