and an increase in free zinc. Redox stress is thought to affect many intracellular metabolic processes including inhibition of reductases and, ultimately, induction of cell death. Oxidative stress induced by MGd appears to exceed the NRF-2 mediated antioxidant capacity in A549 lung cancer cells. The mechanism of action and activity of MGd may be particularly well suited for therapy of NSCLC.

P3-033 **NT: Molecular Therapeutics Posters, Wed, Sept 5 – Thur, Sept 6**

Serum biomarkers predict response to combination celecoxib and erlotinib therapy in advanced non-small cell lung cancer

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Background: Cyclooxygenase-2 (COX-2) overexpression may mediate resistance to EGFR TK inhibition through prostaglandin E2 (PGE2)-dependent promotion of epithelial to mesenchymal transition (EMT). The suppression of epithelial markers such as E-cadherin can to non-small cell lung cancer (NSCLC) resistance to erlotinib. In addition, PGE2 can downregulate E-cadherin expression by upregulating the transcriptional repressors of E-cadherin, ZEB1 and Snail. These findings suggest that COX-2 inhibition may enhance the efficacy of EGFR TKI therapy in NSCLC, and markers of EMT may be important in predicting response to this combination of targeted therapy.

Methods: A phase I, dose escalation trial to was performed investigating the combination of celecoxib and erlotinib in patients with advanced NSCLC. Soluble E-cadherin was evaluated by ELISA in patient serum at baseline and weeks 4 and 8 of treatment. Other markers of COX-2 gene expression and EMT were evaluated by ELISA, including matrix metalloproteinase (MMP)-9, MMP-2, tissue inhibitor of MMP (TIMP1), and CCL15.

Results: 22 patients had serum samples available for evaluation. Serum E-cadherin, MMP-9, MMP-2, TIMP1 and CCL15 were analyzed according to best response (PR, SD or PD). We found a significant decrease in soluble E-cadherin between baseline and week 8 in pts with PR when compared to those with SD or PD ($p = 0.021$). In patients who responded to the combination therapy, baseline MMP-9 was significantly lower compared to non-responders ($p = 0.006$). MMP-2 and TIMP1 showed no significant change based on patient response, and CCL15 decreased in patients with PR.

Conclusions: Soluble E-cadherin, MMP-9 and other downstream markers of COX-2 gene expression may be useful for assessing response to combination celecoxib and erlotinib in pts with advanced NSCLC. A randomized Phase II trial is planned comparing erlotinib and celecoxib with erlotinib plus placebo in advanced NSCLC, to evaluate the efficacy of this combination therapy and to assess these and other biomarkers in both serum and tumor tissue.

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P3-034 **NT: Molecular Therapeutics Posters, Wed, Sept 5 – Thur, Sept 6**

Combined 131I-chTNT and external irradiation for solid tumors in the mouse

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Objective: To compare the difference of only 131I-chTNT and combined 131I-chTNT and external irradiation for solid tumors in the mouse.

Methods: chTNT-3, a chemic monoclonal antibody directed cell nucleus in the necrotic parts of tumor, can play important roles in many tumors. chTNT-3 is iodinated with 131I. Among twenty-four nude mice with tumor cells xenografts(human adenocarcinoma of lung) used in the study, were divided into six groups and given different treatment protocols. Total accumulated dose, 24h percentage of injected activity per gram of tumor tissue and accumulated dose per injected activity were compared between there different groups.

Results: In the study, better yields in terms of total accumulated dose, 24h percentage of injected activity per gram of tumor tissue and accumulated dose per injected activity were seen in the first group.

Conclusions: Enhanced effects can be achieved by combined external irradiation with radioimmunotherapy using the monoclonal anticytokeratin antibody 131 I-chTNT. 20Gy of external irradiation should be given prior to Mab injection.

P3-035 **NT: Molecular Therapeutics Posters, Wed, Sept 5 – Thur, Sept 6**

soluble vascular endothelial growth factor receptor 1(s VEGFR1) transducted by sendai virus using dendritic cells as vector inhibited HUVEC activity in vitro and growth and metastasis of Lewis lung cancer in vivo

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Objective: To evaluate the anticancer effect of s VEGFR1 transducted by sendai virus using dendritic cells(DCs) as vector in vitro and in vivo

Methods: Isolated and purified mouse bone marrow derived DCs were infected by sendai viruses at different moi, which were transducted by s VEGFR1(s VEGFR1-SeV-DCs). The culture medium was collected to treat HUVEC in vitro to analysis the proliferation, apoptosis, s VEGFR1-SeV-DCs were injected to Lewis lung cancer bearing mice to evaluate the survival time, growth and metastasis in vivo.

Results: s VEGFR1-SeV-DCs inhibited the proliferation of HUVEC, and induced apoptosis in vitro, s VEGFR1-SeV-DCs inhibited the growth and metastasis of Lewis lung cancer in vivo, and inhibited proliferation of lung cancer, induced apoptosis of cancer cells and inhibited the angiogenesis and improved immunological response.

Conclusions: SeV-DC was an effective vector in immuno-gene therapy, s VEGFR1 was an interesting gene in gene therapy, it is need to be studied further in future.

P3-036 **NT: Molecular Therapeutics Posters, Wed, Sept 5 – Thur, Sept 6**

Combination of low-dose chemotherapy with intratumoral dendritic cell vaccine is beneficial for the treatment of murine non small cell lung cancer

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At present study, we evaluated an antitumor potential of low- dose chemotherapy combined with intratumoral dendritic cells (DC) vaccine in the s.c. murine Lewis lung cancer model. The dose of chemotherapeu-