Gene Signature for Immunotherapy Response Prediction in Cancer Based on Nuclear Factor-kappa B

This technology is a ten-gene signature that correlates nuclear factor-kappa B (NF-κB) activity with potential for immunotherapy response. Our mouse studies demonstrated a direct link between increased NF-κB activity in tumors and immune cell killing of implanted tumors. This led to the development of a gene signature based on NF-κB activation. In human lung and melanoma patient samples, this signature correlates with increased recruitment of T-cells to tumors, suggesting that these tumors would respond favorably to cancer immunotherapy.

COMMERCIAL OPPORTUNITY

- The potential market for a gene signature in cancer immunotherapy is exemplified by ipilumumuab that is approved for metastatic melanoma with annualized sales of $648MM. Predicting patient response to ipilumumab could potentially save insurance payers $115,000 per patient because ipilumumab only has responses in 25% of patients treated and 80-90% of those will eventually relapse soon after therapy.
- Several additional cancer immunotherapies are in development, such as BMS-936558, BMS-936559, BMS-663513(BMS), CT-011(Curetech), MK-3475(Merck), CP-870893(Pfizer), which represent a large growth potential in the market if our signature shows utility in predicting response to these therapies.
- BMS-936558 showed response rates similar to ipilumumab in a Phase I clinical trial in advanced melanoma (28%), non-small cell lung cancer (18%), and renal cancer (27%), thereby demonstrating a similar need for patient response prediction.
- Currently there is no approved gene signature for prediction of response to cancer immunotherapy and our gene signature can be measured using patient tumor biopsy samples, allowing easy integration into the current melanoma, lung and breast cancer diagnostic protocols.

TECHNOLOGY

Our initial studies showed that lung or breast tumor cells that expressed overactive NF-κB were rejected by the immune system of immune-competent mice. To capitalize on this phenomenon, we then developed a novel gene signature based on genes that were differentially expressed in cells with overactive versus inhibited NF-κB. This gene signature could be used as a biomarker for tumors that have highly active NFκB and therefore have a greater chance of shrinking in response to immune system-boosting immunotherapy drugs. Our studies in human patient samples showed that increased expression of our signature correlated well with T-cell recruitment to lung (correlation constant=0.79) and melanoma (r=0.92) primary tumors, which was a surrogate marker for potential tumor recognition and killing by the immune system. Studies correlating the signature to cancer therapy response are in development and the signature is currently being optimized for use on paraffin embedded tissues.

PUBLICATION/PATENT

- PCT application filed on 11/01/2012 for Drs. Beg, Enkemann and Chen

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11MB069.2012.11