

Why should we analyze analyte fluorescence instead of concentration for multiplex immunoassays?**Edmond J Breen**

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Tissue samples (plasma, saliva, serum or urine) from 169 patients classified as either normal or having one of seven possible diseases (COPD, Mono, Myeloma, Psoriasis, RA, Sepsis and T2D) are analyzed across three 96-well plates for the presences of 37 analytes using cytokine inflammation multiplexed immunoassay panels. Censoring for concentration data caused problems for analysis of low abundant analytes. Using fluorescence analysis over concentration based analysis allowed analysis of these low abundant analytes. Mixed-effects analysis on the resulting fluorescence and concentration responses reveals a combination of censoring and mapping the fluorescence responses to concentration values, through a 5PL curve, changed observed analyte concentrations. Simulation verifies this, by showing a dependence on the mean fluorescence response and its distribution on the observed analyte concentration levels. Differences from normality, in the fluorescence responses, can lead to differences in concentration estimates and unreliable probabilities for treatment effects. It is seen that when fluorescence responses are normally distributed, probabilities of treatment effects for fluorescence based t-tests has greater statistical power than the same probabilities from concentration based t-tests. We add evidence that the fluorescence response, unlike concentration values, doesn't require censoring and it is seen with respect to differential analysis on the fluorescence responses that background correction is not required.

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The role of micro-RNAs as predictors of response to Tamoxifen treatment in breast cancer patients**Emiel Janssen**

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endocrine therapy, via tamoxifen or aromatase inhibitor, is a key treatment strategy to control and eradicate breast cancer. However, resistance to endocrine therapy leads to breast cancer relapse. The recent extension of adjuvant tamoxifen treatment up to 10 years actualizes the need for monitoring breast cancer development during treatment. MicroRNAs are promising biomarkers that may fill the gap between preclinical knowledge and clinical observations regarding endocrine resistance. MicroRNAs regulate gene expression by posttranscriptional repression or degradation of mRNA, most often leading to gene silencing. MicroRNAs have been identified directly in the primary tumor, but also in the circulation of breast cancer patients. The few available studies investigating microRNA in patients suggest that seven microRNAs (miR-10a, miR-26, miR-30c, miR-126a, miR-210, miR-342 and miR-519a) play a role in tamoxifen resistance. Ingenuity Pathway Analysis (IPA) reveals that these seven microRNAs interact more readily with oestrogen receptor (ER) independent pathways than ER-related signaling pathways. Some of these pathways are targetable (e.g. PIK3A) suggesting that microRNAs as biomarkers of endocrine resistance may have clinical value. Validation of the role of these candidate microRNAs in large prospective studies is warranted. Currently a microRNA profiling study has been performed in ER-pos breast cancer patients with and without recurrences under tamoxifen treatment. Results from the literature and the profiling studies will be compared with each other.

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