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Detection of cancer associated glycan on different circulatory glycoproteins with lectin coated on europium nanoparticles

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Background: The great majority of circulating cancer biomarkers are non-specific as substantial overlap in concentrations may be found with samples from healthy subjects and patients with benign diseases. Thus, most of them are used only for follow-up of the disease and monitoring the treatment. Cancer markers are mostly glycoproteins and aberrant glycosylation is a universal feature of cancer cells. Detection of cancer-related glycosylation changes is highly attractive for early cancer detection. Lectins are carbohydrate-binding proteins and can be exploited for specific recognition of these changes. We have established a lectin library, where individual lectins with known glycostructure specificity are immobilized onto fluorescent Europium-chelate-doped 97 nm nanoparticles (Eu+3-NPs) making them multivalent and highly reactive toward the target. The library was used for screening of multiple glycoprotein markers isolated from benign and malignant sources. Using lectin-coated Eu+3-NPs, analytically sensitive cancer associated glycoprotein-lectin assays were developed that specifically recognize the isoforms of cancer biomarkers produced by cancer cells, whereas the detection of glycoproteins from benign conditions was reduced. This approach has been applied for CA125, CA15-3, PSA, CA19.9 and CEA derived from ovarian, breast, prostate, pancreatic and colon cancer specific cell line, respectively. Interestingly, we successfully translated the cell line antigen based data to clinical samples in some of the cancers mentioned here. The improved analytical specificity of this test approach is dependent on a discriminating lectin immobilized in large numbers on Eu+3-NPs, providing both an avidity effect and signal amplification. Finally, using appropriate combinations of lectins and antibodies, applying the lectin NPs concept can also be explored for other diagnostic targets, where changes in glycosylation are indicative of an ongoing disease process. In this seminar, I will discuss the methodology we developed to make small library of lectin-nanoparticles for screening of cancer associated circulating glycoprotein in clinical serum samples. And how, in our more recent work, we have used the new generation of lectin-nanoparticle assisted immunoassay in cancer specific assay development? It is expected that the technical approach is transferable to a wide range of other existing and novel cancer biomarkers.

Biography

Kamlesh Gidwani has his expertise in the development and improvement of cancer specific diagnostics. His lectin Eu+3- nanoparticles model for detection of cancer associated glycans creates new pathways for improving healthcare. He has built this model after years of experience in research and evaluation, and applied this model in different cancer specific biomarker development. His recently published paper in Clinical Chemistry was further highlighted in the journal in the form of a Clinical Chemistry's Podcast and journal club.

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