OPEN ACCESS Freely available online

ISSN: 2153-0602
Journal of
Data Mining in
Genomics & Proteomics

Commentary

Papillary RCC Biomarkers and the Proteogenomics of Activating *MET* Mutations

Danielle Stanley*

Department of Molecular Genetics, Indiana University School of Medicine, Indianapolis, Indiana, USA

DESCRIPTION

Papillary Renal Cell Carcinoma (pRCC) is the second most common subtype of kidney cancer, accounting for about 15% of all Renal Cell Carcinoma (RCC) cases. It differs from the more prevalent clear cell RCC in both its histological appearance and molecular characteristics. A growing body of research has identified main biomarkers and genetic alterations associated with pRCC, which have important implications for its diagnosis, prognosis and treatment. One of the most significant discoveries is the role of mutations in the *MET* gene, particularly activating mutations, in the pathogenesis of pRCC. Proteogenomics, the integrated study of genomics and proteomics, has become an important approach for understanding the impact of these *MET* mutations, providing novel insights into disease mechanisms and identifying potential therapeutic targets.

Papillary RCC and its subtypes

Papillary RCC is divided into two subtypes, pRCC Type 1 and pRCC Type 2, based on histological and molecular differences. Type 1 pRCC is typically associated with better prognosis and characterized by small, basophilic cells arranged in a papillary architecture. Type 2 pRCC, on the other hand, is more aggressive, with larger, eosinophilic cells and is often associated with worse clinical outcomes.

Understanding the molecular differences between these two types has been a main focus of research, with *MET* mutations emerging as a critical driver, particularly in Type 1 pRCC. In both subtypes, however, various biomarkers have been identified that can aid in diagnosis, predict response to treatment and provide insight into patient prognosis.

MET mutations in papillary RCC

The *MET* gene encodes a receptor tyrosine kinase known as the Hepatocyte Growth Factor Receptor (HGFR). Under normal conditions, *MET* signaling plays a critical role in cellular processes such as growth, survival and migration. However, activating mutations in the *MET* gene can lead to aberrant signaling, which promotes tumorigenesis and cancer progression. In the context of pRCC, *MET* mutations are most commonly associated with Type 1 pRCC but can also be present in sporadic cases of Type 2 pRCC.

Germline and somatic *MET* mutations: Germline *MET* mutations have been identified in patients with Hereditary Papillary RCC (HPRC), a familial syndrome that predisposes individuals to developing bilateral, multifocal Type 1 pRCC. These mutations lead to constitutive activation of *MET*, resulting in unchecked cellular proliferation. Somatic *MET* mutations, occurring sporadically, are also observed in a significant proportion of pRCC cases, particularly in Type 1. These mutations are considered activating because they induce ligand-independent activation of the *MET* receptor, driving oncogenic pathways.

***MET* overexpression and amplification:** In addition to point mutations, *MET* overexpression and gene amplification have been observed in pRCC, particularly in advanced or metastatic cases. This suggests that *MET* dysregulation plays a multifaceted role in pRCC pathogenesis, making it a compelling therapeutic target for *MET* inhibitors.

Proteogenomics: Insights into *MET*-driven pRCC

Proteogenomics integrates genomic data (such as DNA and RNA sequencing) with proteomic analysis (the study of protein expression, modification and function) to provide a comprehensive view of how genetic alterations, like *MET* mutations, manifest at the protein level. This approach is particularly valuable in cancer research, as it links genetic mutations to their downstream effects, including protein activation, signaling pathway changes and metabolic reprogramming.

Correspondence to: Danielle Stanley, Department of Molecular Genetics, Indiana University School of Medicine, Indianapolis, Indiana, USA, E-mail: standanieljunior4@gmail.com

Received: 24-Aug-2024, Manuscript No. JDMGP-24-27277; **Editor assigned:** 26-Aug-2024, PreQC No. JDMGP-24-27277 (PQ); **Reviewed:** 09-Sep-2024, QC No. JDMGP-24-27277; **Revised:** 16-Sep-2024, Manuscript No. JDMGP-24-27277 (R); **Published:** 23-Sep-2024, DOI: 10.4172/2153-0602.24.15.353

Citation: Stanley D (2024). Papillary RCC Biomarkers and the Proteogenomics of Activating *MET* Mutations. J Data Mining Genomics Proteomics. 15:353.

Proteomic insights into *MET*-driven pathways: By using proteogenomics to study pRCC samples with *MET* mutations, researchers have uncovered alterations in multiple signaling pathways that contribute to tumor growth and metastasis. For example, the *MET* signaling axis involves the PI3K/AKT and MAPK pathways, both of which are known to promote cell survival and proliferation. Proteomic studies have shown that activating *MET* mutations result in hyperactivation of these pathways, leading to increased levels of phosphorylated proteins that drive oncogenic signaling.

Phosphoproteomics and *MET* activity: One of the most potential proteogenomic tools in cancer research is phosphoproteomics, which specifically looks at protein phosphorylation events that regulate major signaling pathways. In *MET*-mutated pRCC, phosphoproteomic analysis has revealed aberrant phosphorylation patterns in proteins involved in cell motility, invasion and survival. This highlights the role of *MET* in promoting not only tumor growth but also metastatic spread, making it an important target for therapeutic intervention.

Metabolic reprogramming in *MET*-mutated pRCC: Proteogenomics has also explain the metabolic changes that occur in pRCC as a result of *MET* mutations. Tumor cells with activated *MET* signaling often exhibit increased glucose uptake, enhanced glycolysis and altered lipid metabolism sign of the metabolic reprogramming that supports rapid cell growth and survival under the hypoxic conditions typically found within tumors. These insights provide potential new targets for metabolic therapies aimed at disrupting the altered energy production pathways in *MET*-driven pRCC.

Biomarkers for diagnosis and therapeutic response

The identification of biomarkers associated with MET mutations and their downstream effects has significant clinical implications. These biomarkers can be used for diagnosing pRCC, predicting patient outcomes and guiding treatment decisions.

MET as a diagnostic biomarker: MET expression and mutation status help diagnose Type 1 pRCC and differentiate it from other RCC subtypes, especially when histological features are unclear.

Predicting response to MET inhibitors: MET inhibitors (e.g., cabozantinib, crizotinib) are effective in treating MET-mutated pRCC. Proteogenomics can identify patients likely to respond by analyzing MET activation and monitor treatment through protein changes.

Prognostic biomarkers: Proteins involved in MET signaling, particularly those related to cell migration and invasion, are linked to aggressive disease and poor prognosis, serving as valuable prognostic markers in pRCC.

Future directions in MET-driven pRCC research

The integration of proteogenomics into pRCC research is poised to accelerate the development of personalized medicine approaches. By understanding how specific *MET* mutations affect protein expression and signaling pathways, researchers can design more effective therapeutic strategies that target the unique molecular characteristics of each patient's tumor. Furthermore, as proteogenomic technologies continue to advance, they may reveal novel biomarkers and therapeutic targets that could improve the diagnosis, treatment and overall survival of pRCC patients.