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Role of insulin-like growth factor-1 (IGF-1) in IgA-mediated nephropathy: *Ex vivo* studies on rat glomerular mesangial cells

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Background: IgA nephropathy (IgAN) is a common renal disorder among children worldwide, including Kuwait. Glomerulonephritis due to mesangial proliferation is responsible for renal dysfunction in IgAN, however molecular mechanisms of pathogenesis are not well known. In this study, we explore the role of insulin-like growth factor-1 (IGF-1), a potent mitogen with vital role in growth and development of children, in pathogenesis of IgAN using cultures of glomerular mesangial cells (GMC).

Methods: GMC were isolated from rat kidneys using sieving and enzymatic digestion of tissue homogenates, and cultured in RPMI 1640 medium. GMC culture was treated with IgA (0-10 ug.ml) in the presence or absence of IGF-1, platelet-derived growth factor (PDGF), epidermal growth factor (EGF) and basic fibroblast growth factor (bFGF).

Results: Treatment of GMC with IgA (5 -10 ug) significantly increased the BrdU incorporation in a serum/mitogen-free medium and also markedly potentiated IGF-1-/PDGF-induced DNA synthesis. IgA was observed to significantly increase the levels of IGF-1 in culture supernatants with no marked effect on PDGF content.

Conclusion: These findings show that IgA enhances the IGF-1 activity in GMC and suggest a role for IGF-1 in pathogenesis of IgAN.

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Clinical utility of whole exome sequencing for genetic diagnosis of autosomal dominant polycystic kidney disease

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Autosomal Dominant Polycystic Kidney Disease (ADPKD) is an inherited renal disease characterized by the accumulation of clusters of fluid-filled cysts in the kidneys with reported incidence ranging between 1:400 and 1:1000 worldwide. ADPKD is caused by mutations in two genes; *PKD1*, which account for around 85% of all reported ADPKD cases and *PKD2*. Genetic analysis and mutation screening of ADPKD cases are more technically challenging compared to other monogenic diseases as *PKD1* lies in a segmentally duplicated region, such that the first 32 exons are replicated 6 times in pseudo genes located in regions 13-16 Mb proximal to the original *PKD1* (16p.13.1) and share between 97.6% to 97.8% sequence homology to the *PKD1* gene [16-18]. As these pseudo-regions are less amenable to selection pressure they tend to have high mutation rates when compared to the parent gene. These duplicated regions represent a diagnostic challenge for ADPKD as conventional sequencing is not effective in specifically targeting the genuine *PKD1* regions. The development of next generation sequencing (NGS) platforms allowed facilitated faster sequencing of a higher DNA throughput at lower cost in comparison to traditional Sanger sequencing which encouraged wider utilization of such technologies in the medical field. In this study, we evaluate the efficiency of Whole Exome Sequencing (WES) in sequencing *PKD1* and *PKD2* for detecting ADPKD mutations in patients who were clinically evaluated by ultrasonography. Our results highlight the advantages and limitations of WES in ADPKD genetic diagnosis.

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