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Acute, renally restricted siRNA-mediated gene silencing/adeno-associated virus gene rescue through a novel Renal Subcapsular approach

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Abstract

Gene silencing has led to important discoveries in the roles of genes but competing or compensatory systems in conventional knockout can occur during development. The role of a certain gene on the function of specific tissues can also be studied by tissue specific gene silencing which could be made inducible but not reversible. The role of genes of interest on the physiology of one kidney can be studied by doing cross-renal transplantation but this procedure is laborious and costly. Selective gene silencing in one or both kidneys can be done in mice by the renal subcapsular infusion of siRNA or shRNA. This method allows the silencing of the gene(s) of interest in the ipsilateral kidney and studying the consequences of this maneuver in the contralateral kidney (efficiency ≈ 40-70% in the renal cortex only). Gene expression reverts back to normal levels after 7 days from cessation of siRNA infusion. siRNA gene silencing should be complemented by the renal subcapsular infusion of AAV vectors. The infusion of such viral vectors retrogradely via the ureter affords gene silencing in the renal medulla. The silencing of genes in other organs of interest can also be done by the infusion of siRNA into the artery that supplies the organ of interest, so long as blood supply is not impeded. Our novel subcapsular or arterial siRNA or AAV infusion offers the advantage of restricted gene silencing or rescue of the gene of interest in one kidney only or the organ of interest.

Biography

Pedro A. Jose received his M.D. degree, magna cum laude, from the University of Santo Tomas, Philippines and received his Ph.D. degree in Physiology from Georgetown University. He has published more than 330 articles; 4 as covers of scientific journals and 5 as subject of editorial commentaries. His research has been recognized (2007 Ernest H. Starling Lecture, 2003 Lewis K. Dahl Memorial Lecture, and NIH MERIT Award). Deciphering the role of variations of the *GRK4* in the causation of human essential hypertension was cited by the Director of the NHLBI for its FY 2004 Budget Justification to the US Congress.