The Novel Mutation in the Steroidogenic Acute Regulatory Protein (StAR) in 46, XY Case with Adrenal Insufficiency and Complete Sex Reversal

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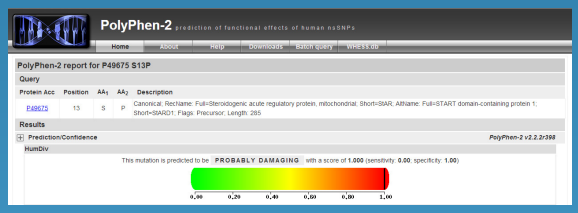
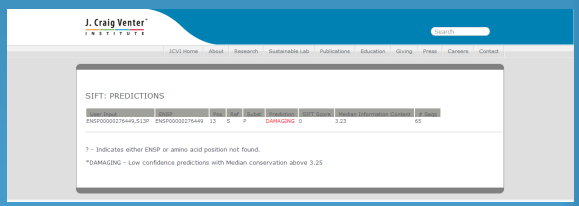
Background:
The steroidogenic acute regulatory protein (StAR) has been shown to be essential for steroidogenesis by mediating cholesterol transfer into mitochondria. Inactivating StAR mutations cause the typical clinical picture of congenital lipoid adrenal hyperplasia. Lipoid congenital adrenal hyperplasia is a rare autosomal recessive disorder that is characterized by diminished or absent adrenal and gonadal steroid hormone biosynthesis. Patients present with adrenal insufficiency and typically with complete sex reversal in 46,XY.

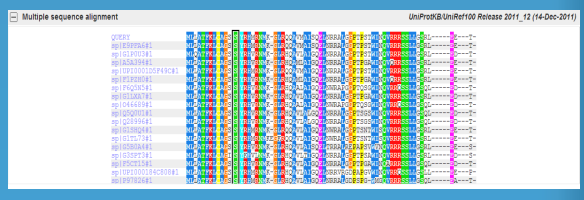
Objective and Method:
We aimed to identify causative mutations in cases presenting with adrenal failure during early infancy. Consecutive cases with adrenal failure during early infancy were studied. The coding regions of the StAR gene (uc003xkv.1) is PCR-amplified and automatedly sequenced.

Patient:
The term neonate weighing 3000 g was born as the second child to healthy first degree consanguineous parents. Neither neonatal hypoglycemia nor respiratory distress was detected. Newborn screening for congenital adrenal hyperplasia was not performed. At the third month of life the child presented with acute crises including vomiting, dehydration, hypotension, hyponatremia, and hyperkalemia. Her family history suggested that two previous siblings had a very similar clinical condition and died at the age of 9th and 14th months. Clinical examination revealed normal female external genitalia with mild hyperpigmentation of the skin. Inguinal gonads were palpable. Laboratory investigations revealed severe hypocortisolemia and extremely elevated ACTH and plasma renin activity consistent with primary adrenal insufficiency (Table1). Karyotype analysis was 46,XY. A pelvic MRI demonstrated the absence of Mullerian structures. Patient was diagnosed with lipoid CAH and started hydrocortisone and fludrocortisone replacement therapy.

Case	
Presentation age	3 months
Consanguinity	present
Prader stage	1
Mullerian structures absent	(+)
Chromosome	46,XY
Na (mmol/L)	115
K (mmol/L)	5.9
17-OH Progesterone (ng/ml)	0.02
ACTH (pg/ml)	> 1250
Cortisol (µg/dL)	3.43
Testosterone (ng/dl)	<2
Plasma renin activity (ng/ml/s)	100
17-OH pregnalonone (ng/dl)	<0.1
Mutation	S13P homozygous







Results:
A homozygous state consisting of p.S13P was detected in a patient. Functional studies of the new mutations are ongoing.

Conclusion:
The novel mutation of p.S13P cause early infancy adrenal insufficiency and complete sex reversal in the 46, XY case.