

## **Mainzer-Saldino syndrome is a ciliopathy caused by mutations in the IFT140 gene**

Isabelle Perrault, Sophie Saunier, Sylvain Hanein, Emile Filhol, Albane Bizet, Felicity Collins, Mustafa Salih, Eduardo Silva, Véronique Baudouin, Machteld Oud, et al.

► **To cite this version:**

Isabelle Perrault, Sophie Saunier, Sylvain Hanein, Emile Filhol, Albane Bizet, et al.. Mainzer-Saldino syndrome is a ciliopathy caused by mutations in the IFT140 gene. First International Cilia in Development and Disease Scientific Conference, pp.O28. inserm-00752958

**HAL Id: inserm-00752958**

**<https://www.hal.inserm.fr/inserm-00752958>**

Submitted on 16 Nov 2012

**HAL** is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

ORAL PRESENTATION

Open Access

# Mainzer-Saldino syndrome is a ciliopathy caused by mutations in the *IFT140* gene

I Perrault<sup>1\*</sup>, S Saunier<sup>2</sup>, S Hanein<sup>1</sup>, E Filhol<sup>2</sup>, A Bizet<sup>2</sup>, F Collins<sup>3</sup>, M Salih<sup>4</sup>, E Silva<sup>5</sup>, V Baudouin<sup>6</sup>, M Oud<sup>7</sup>, N Shannon<sup>8</sup>, M Le Merrer<sup>1</sup>, C Pietrement<sup>9</sup>, P Beales<sup>10</sup>, H Arts<sup>7</sup>, A Munnich<sup>1</sup>, J Kaplan<sup>1</sup>, C Antignac<sup>2</sup>, V Cormier Daire<sup>1</sup>, JM Rozet<sup>1</sup>

From First International Cilia in Development and Disease Scientific Conference (2012)  
London, UK. 16-18 May 2012

## Introduction

Ciliopathies is an emerging class of genetic disorders due to altered cilia assembly, maintenance or function. Syndromic ciliopathies affecting bone development have been classified as skeletal ciliopathies. Mutations in genes encoding components of the intraflagellar transport (IFT) complex A, that drives retrograde ciliary transport, are a major cause of skeletal ciliopathies. Mainzer-Saldino syndrome (MSS) is a rare disorder characterized by phalangeal cone-shaped epiphyses, chronic renal failure and early-onset severe retinal dystrophy.

## Methods and results

We collected 16 families presenting three diagnostic criteria of MSS. Through ciliome re-sequencing combined to Sanger sequencing, we identified *IFT140* mutations in seven MSS families. The effect of the mutations on IFT140 localization was assessed using flagged-IFT140 mutant proteins which showed a partial to nearly complete loss of basal body localization associated with an increase of cytoplasm staining while the wild-type Flagged-IFT140 protein predominantly localized to the basal bodies in RPE1 cells. To assess the impact of *IFT140* mutations on ciliogenesis, abundance and morphology of primary cilia were studied in cultured fibroblasts of patients and detected absent cilia in a high proportion of patient cells compared to controls. Ciliary localization of anterograde IFTs were altered in MSS patient fibroblasts supporting the pivotal role of IFT140 in proper development and function of ciliated cells.

## Conclusion

Here we report on compound heterozygosity or homozygosity for *IFT140* mutations in seven MSS families. After Sensenbrenner and Jeune syndromes, MSS is the ultimate skeletal ciliopathy ascribed to IFT disorganization.

## Author details

<sup>1</sup>INSERM U781 & Department of Genetics, Paris Descartes University, France. <sup>2</sup>INSERM, U983, Paris Descartes University, France. <sup>3</sup>Department of Clinical Genetics, Westmead Hospital, Sydney, Australia. <sup>4</sup>Department of Clinical Genetics, King Khalid University Hospital, Riyadh, Saudi Arabia. <sup>5</sup>Department of Ophthalmology, Coimbra University Hospital, Portugal. <sup>6</sup>Department of Nephrology, CHU Robert Debré, Paris, France. <sup>7</sup>Department of Human Genetics, Radboud University Nijmegen Medical Centre, Nijmegen, the Netherlands. <sup>8</sup>Clinical Genetics Service, City Hospital, Nottingham, UK. <sup>9</sup>Department of Pediatrics, American Memorial Hospital, CHU Reims, France. <sup>10</sup>Molecular Medicine Unit, University College London (UCL) Institute of Child Health, UK.

Published: 16 November 2012

doi:10.1186/2046-2530-1-S1-O28

Cite this article as: Perrault et al.: Mainzer-Saldino syndrome is a ciliopathy caused by mutations in the *IFT140* gene. *Cilia* 2012 1(Suppl 1):O28.

Submit your next manuscript to BioMed Central and take full advantage of:

- Convenient online submission
- Thorough peer review
- No space constraints or color figure charges
- Immediate publication on acceptance
- Inclusion in PubMed, CAS, Scopus and Google Scholar
- Research which is freely available for redistribution

Submit your manuscript at  
[www.biomedcentral.com/submit](http://www.biomedcentral.com/submit)



\* Correspondence: [isabelle.perrault@inserm.fr](mailto:isabelle.perrault@inserm.fr)

<sup>1</sup>INSERM U781 & Department of Genetics, Paris Descartes University, France  
Full list of author information is available at the end of the article