

Processus de sélection - AAPG 2026 Phase 1

ANDROCHOL

Coordinateur du projet

Nom : TANNOUR-LOUET

Prénom : Mounia

Courriel : mounia.tannour-louet@inserm.fr

AVIS FINAL DU COMITÉ

Ce rapport final doit permettre au coordinateur / à la coordinatrice scientifique de comprendre la décision collégiale du comité concernant son projet. Merci de veiller à ce que ces commentaires soient soigneusement rédigés, argumentés, relatifs aux seuls critères d'évaluation et aux seuls éléments présents dans la proposition et son annexe (i.e. les CV), sans recommandation, celle-ci ne pouvant être gage de réussite en cas de re-dépôt du projet.

Tel qu'indiqué dans l'engagement de confidentialité signé en ligne, l'utilisation de l'IA n'est pas autorisée pour la rédaction des évaluations:

"Article 1.3 Je prendrai toutes les mesures nécessaires pour préserver le caractère confidentiel des informations et documents et prévenir toute fuite de données. A ce titre je m'engage à ne pas déposer tout ou partie(s) de ces données dans des outils d'IA (notamment ChatGPT) ou des outils utilisant l'IA (comme DeepL) pour conduire l'évaluation et/ou rédiger mon rapport d'évaluation."

QUALITE ET AMBITION SCIENTIFIQUE - critère discriminant: nécessité d'obtenir une notation A de la part du comité à ce critère pour passer en étape 2 -

- Clarté des objectifs et des hypothèses de recherche
- Ambition scientifique du projet et positionnement par rapport à l'état de l'art [plus-value du projet en termes d'apport scientifique - objet, problématique, approche méthodologique - et en termes de production de connaissances]
- Adéquation et pertinence des méthodes mises en œuvre [incluant la couverture mono- trans-inter- disciplinaire]
- Adéquation du projet à l'axe scientifique choisi

NOTE

A

COMMENTAIRE

The objectives of the project are clearly articulated and built around a strong and coherent central hypothesis, that VAMP7-dependent vesicular trafficking coordinates intracellular and intercellular cholesterol fluxes required for androgen production, epididymal signaling, and sperm membrane remodeling, and that disruption of this pathway underlies a previously unrecognized mechanism of androgen insensitivity and male infertility. The project logic is well structured, progressing from mechanistic cellular studies to organoid-based functional analyses, in vivo mouse validation, and human genetic investigations. The hypotheses are explicit, biologically plausible, and well supported by extensive preliminary data.

The project is highly ambitious and addresses a major unresolved question in male reproductive physiology: how normal systemic androgen levels can coexist with defective local androgen action and

impaired spermatogenesis. By positioning VAMP7 at the intersection of cholesterol trafficking, endolysosomal secretion, and androgen responsiveness, the proposal introduces a novel conceptual framework that goes beyond canonical androgen receptor-centric models of androgen insensitivity. The integration of cholesterol homeostasis, vesicular trafficking, and epididymal exosome biology represents a significant advance over the current state-of-the-art. The originality of the project is reinforced by the combination of unique genetic models (VAMP7 KO/OE mice), state-of-the-art 3D epididymal organoids, and well-characterized human cohorts, placing the project in a highly competitive but clearly leading position.

The methodological strategy is comprehensive and well aligned with the objectives. The use of advanced imaging (confocal, STED, CLEM), lipidomics, proteomics, live-cell cholesterol tracking, organelle contact site analysis, and functional androgen responsiveness assays provides a robust and multidimensional experimental framework. To note, the project comprises four work packages, which are relatively heavy and will need sufficient resources and budget. Also, probably due to limited space, characterization of epididymal organoids and discussion of VAMP7 expression and potential associated functions in other tissues than reproductive organs are not provided.

The project fits within the C.05 theme, as it addresses physiological and pathophysiological mechanisms underlying steroidogenesis, sperm maturation, and male fertility. The strong translational component, linking fundamental mechanisms to human androgen insensitivity syndromes and idiopathic male infertility, further strengthens its relevance.

ORGANISATION ET REALISATION DU PROJET

- Compétence, expertise et implication du coordinateur / de la coordinatrice scientifique
- Qualité du consortium et complémentarité des contributions

COMMENTAIRE

The project coordinator has a strong expertise in the field of the research project. She has identified VAMP7 mutations as causal factors for AIS in humans and mice; she has previously successfully coordinated research programs. The consortium brings together internationally recognized experts in vesicular trafficking, lysosome biology, steroid signaling, reproductive organoids, and clinical andrology. The complementarity between partners is excellent, with clear task allocation and strong methodological synergy. All three partners have provided strong preliminary data that support the feasibility of the project. The involvement of partners with access to unique patient cohorts and patented organoid technologies significantly enhances the translational potential of the project. The consortium is well balanced and fully appropriate for a collaborative PRC project.

AVIS GENERAL incluant les points forts et les points faibles du projet

Appréciation finale :

- A « Projet invité en étape 2 »
- B « Projet non retenu pour passage en étape 2 »

NOTE
A

COMMENTAIRE

Overall, ANDROCHOL is an excellent project which focuses on sex development disorders and male infertility. It explores novel molecular actors in androgen biosynthesis and signalling pathways. The research hypotheses and objectives are clearly described and supported by strong and exhaustive preliminary data. The project is a clear physiology/pathophysiological project; the methodology includes innovative approaches such as advanced imaging, lipidomics, and 3D epididymal organoids together with genetically engineered mice that reproduce human phenotype. The clinical relevance of the project is evidenced by genetic analyses and characterization of patient cohorts together with investigation of therapeutic strategies of male infertility. The project coordinator has a strong track record in molecular endocrinology, lipid metabolism, and disorders of sex development. Her leadership experience, scientific visibility, and access to high-level infrastructures are clearly demonstrated. The consortium is excellent and

brings complementary expertise associated with excellent track records and scientific recognition of the partners.

CONFIDENTIEL