ROLE OF ACTIN REGULATORS IN HIV-1, IAV, & SARS-CoV-2 VIRUS-LIKE PARTICLES PRODUCTION

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Manon Gourdelier[1], Peggy Merida[1], Jitendrya Swain[1] and Delphine Muriaux[1]

[1]Institut de Recherche en Infectiologie de Montpellier (IRIM), UMR9004, CNRS & Université de Montpellier, Montpellier.

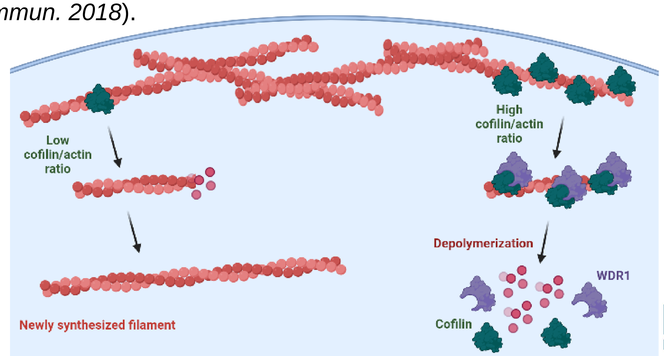
BACKGROUND

HIV-1 IAV/H1N1/pdm09 SARS-CoV-2

My project is to study RNA enveloped viruses which assemble and bud from host cell membrane under which the cortical actin is located.

Are some actin regulatory factors involved in viral production ?

Cofilin was described to be involved in HIV-1 and IAV replication (*Wu et al., 2008, Retrovirology; Liu et al., 2014, Biochem Biophys Res Commun),* and its cofactor WDR1 is involved in actin dynamics by breaking actin (*Shoichiro Ono. Biochem Biophys Res Commun. 2018*).

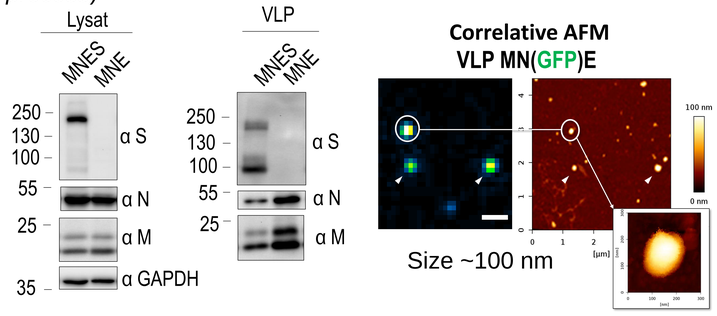


Are Cofilin and WDR1 involved in the assembly and budding of HIV-1, IAV or SARS-CoV-2 particles?

METHODS

1) **Production and purification of VLPs** for the 3 viruses in HEK293T cells : HIV-1 Gag VLP (*Fuller al., 1997, Curr Biol*), IAV VLP (*Kerviel et al., 2016, PLoS One*) and SARS-CoV-2 MNE VLP (*Swann et al.,2020, Scientific Report).*

Optimized production and description of non-fluorescent and fluorescent SARS-CoV-2 Virus-Like Particles *(Gourdelier et al., in process*)



2) **Functional assays** : siRNA Cofilin and WDR1, Western Blots

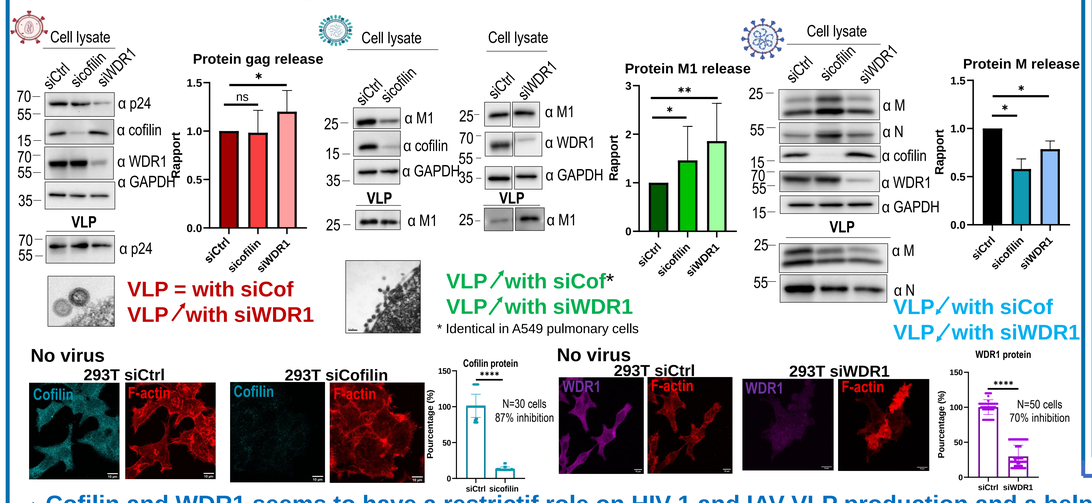
3) **Immunofluorescence** coupled to confocal microscopy to look at cofactors extinction and F-actin localization with siCofilin and siWDR1 and presence of viral proteins.

4) **Immunoprecipitation** to assess complexing between viral proteins and Cofilin or WDR1 cellular proteins.

Cofilin and WDR1 seems to play a different role on **HIV-1** and **IAV** which assemble at cell *plasma membrane* and **SARS-CoV-2** which assemble at *ERGIC*.

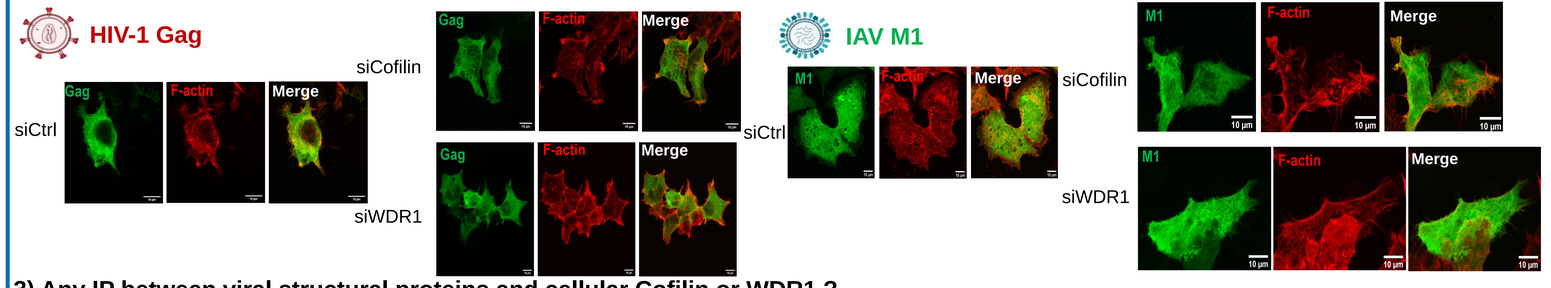
RESULTS

1) Do Cofilin or WDR1 play a role on HIV-1, IAV or SARS-CoV-2 MNE VLP release ?



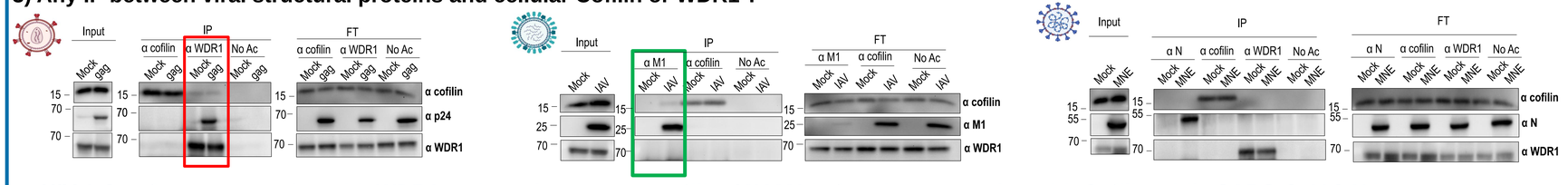
→ Cofilin and WDR1 seems to have a restrictif role on HIV-1 and IAV VLP production and a helping role on SARS-CoV-2 MNE VLP production.

2) Any change of F-actin cellular localization with siCofilin or siWDR1 in the presence of viral proteins ?



→ with siCofilin and siWDR1, HIV-1 Gag or IAV M1 colocalize at the cell plasma membrane with F-actin.

3) Any IP between viral structural proteins and cellular Cofilin or WDR1 ?



→ HIV-1 Gag forms a complex with WDR1 and to a less extend cofilin; IAV-M1 is forming a complex with Cofilin while SARS-CoV-2-N is not.

CONCLUSIONS

- Cofilin and WDR1 are involved in particle production of HIV-1 , IAV and SARS-CoV-2 MNE VLP.
- These actin regulators act differently for HIV-1 and IAV which are budding at the cell plasma membrane and for SARS-CoV-2 particles which are budding at the ERGIC.
- HIV-1 Gag is interacting with WDR1/Cofilin complex and IAV-M1 is interacting with Cofilin. In contrario, WDR1/Cofilin is playing an indirect role in SARS-CoV-2 MNE production.
- Actin dynamic is required for particle production of enveloped viruses most probably via WDR1/Cofilin complex regulation.

PERSPECTIVES

- Confirm interaction, if any, between viral proteins and WDR1 using FRET microscopy.
- Confirm the role of Cofilin and WDR1 on HIV-1 Gag, IAV-M1 and SARS-CoV-2 MNE particle production in infectious systems.

ADDITIONAL KEY INFORMATION

gourdelier.manon@gmail.com → *Find me on LinkedIn*

Looking for a position or a post doc in industry

AKNOWLEDGEMENT

cnrs IRIM MDVA CROI Occitanie Cemipai MRI