

Univerza  
v Ljubljani

Fakulteta *za kemijo*  
*in kemijsko tehnologijo*

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VABILO NA PREDAVANJE  
V OKVIRU DOKTORSKEGA ŠTUDIJA  
KEMIJSKE ZNANOSTI / INVITATION TO  
THE LECTURE WITHIN DOCTORAL  
PROGRAMME IN CHEMICAL SCIENCES

**Prof. Jade Forwood**

*Gulbali Institute  
Charles Sturt University  
Wagga Wagga, NSW, Australia*

z naslovom / title:

**Unravelling Viral Strategies for Innate Immune  
Evasion through Nucleocytoplasmic Transport**

**v sredo, 27. 3. 2024 ob 15. uri /  
on Wednesday, 27. 3. 2024 at 15.00**

**v predavalnici 1 v 1. nadstropju Fakultete za kemijo in  
kemijsko tehnologijo, Večna pot 113 / in lecture room 1,  
1st floor at the Faculty of Chemistry and Chemical  
Technology, Večna pot 113**

*Vljudno vabljeni! | Kindly invited!*

**Abstract:**

The presentation will cover two areas of research.

The emergence of the MERS coronavirus (MERS-CoV) has inspired investigations into its innate immune evasion strategies. One such mechanism involves the ORF4b protein's interaction with nuclear import adapter IMP $\alpha$ 3, inhibiting NF- $\kappa$ B-dependent innate immunity. The presentation will describe high-resolution structures of ORF4b bound to distinct IMP $\alpha$  family members, revealing unconventional binding mechanisms. Mutations within the nuclear localization signal (NLS) region transform the binding mechanism, underlining its significance for nuclear import, IMP $\alpha$  engagement, and innate immune pathway suppression. The study extends to closely related coronaviruses like HKU5, and describes how small ORF4b mutations can alter IMP $\alpha$  interactions.

The presentation will also cover how Hendra and Nipah virus W proteins specifically target isoforms of importin  $\alpha$ . Despite a conserved nuclear localization signal (NLS) recognition region, varying importin  $\alpha$  isoforms interact uniquely with cargoes. The talk will describe the structural underpinnings of W proteins' nuclear import specificity in Hendra and Nipah viruses. Structural analysis of cargo-bound importin  $\alpha$ 1 and  $\alpha$ 3 reveals an expansive interface and greater binding affinity for importin  $\alpha$ 3. This specificity stems from distinctive positioning of regions within the isoforms, validated through chimeric and mutant importin  $\alpha$  constructs and cargo-free isoform structures.

Together, these investigations deepen our comprehension of viral manipulation of nucleocytoplasmic transport for immune evasion and shed light on the nuanced interactions governing cargo-specific import.