# UDP-glucose Glycoprotein Glucosytransferase 1 Deploys from Endoplasmic Reticulum to Cytosol and Associates with Enterovirus 71 3D Polymerase to Facilitate Viral RNA Elongation Activity

Peng-Nien Huang[1*], Jia-Rong Jheng[1], Jim-Tong Horng[1], Shin-Ru Shih[1]

[1.] Research Center for Emerging Viral Infections/Chang Gung University

**Background/Objective**
Enterovirus 71 (EV71) infections associates with severe neurological diseases in children. It has caused numerous outbreaks with mortalities worldwide. The 3D RNA-dependent RNA polymerase (RdRP) of EV71 is a crucial component of viral replication. The function of the 3D polymerase is to replicate viral genomic RNA. This study aimed to identify the cellular proteins that interact with 3D polymerase and to evaluate the significance of such the interactions in EV71 replication.

**Method**
We used immunoprecipitation to purify the 3D-interacting proteins from an EV71-infected cell lysate, and used matrix-assisted laser desorption/ionization-time of flight (MALTDI-TOF) mass spectrometry for protein identification.

**Result**
We identified that endoplasmic reticulum (ER) protein UDP-glucose glycoprotein glucosyltransferase 1 (UGGT1), a selectively unfolded glycoprotein that functions in folded proteins quality control, associates with 3D polymerase. We verified the 3D-UGGT1 interaction using co-immunoprecipitation and confocal microscopy. UGGT1 expression level is increased, and UGGT1 is distribution from ER lumen to cytosol interacting with 3D polymerase during EV71 infection. Replication of EV71-Luc replicon and virus growth curve assays showed that the cellular factor UGGT1 is a positive regulator of EV71 replication. We then performed 3D polymerase activity assays in vitro, with results indicating that UGGT1 facilitates viral RNA synthesis by accelerating 3D polymerase elongation activity but not uridylylation activity.

**Conclusion**
Host protein UGGT1 may serve as a potential therapeutic target for the control of viral replication.