43RD ANNUAL MEETING OF THE EUROPEAN SOCIETY FOR PAEDIATRIC INFECTIOUS DISEASES
BUCHAREST & ONLINE 26-30 MAY 2025 #ESPID2025

EV0809 / #2361

PREVENTION AND CONTROL OF HUMAN NOROVIRUS INFECTION: COST-EFFECTIVE SYSTEM FOR VACCINE-GRADE VP1 SYNTHESIS

PUBLIC HEALTH AND EPIDEMIOLOGY (ONLY NON-SARS-COV2 CONTENT): POPULATION STUDIES AND SURVEILLANCE

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Background: Human norovirus (NoV) is the leading cause of acute gastroenteritis in all age groups and is often linked to large outbreaks. It is responsible for approximately 70,000 deaths in children globally per year. There are still no licensed vaccines for NoV infection prevention and control. The vaccine development faces challenges due to the high antigenic diversity of the virus and its uncultivable nature. Virus-like particles (VLPs) based on the self-assembled major capsid protein VP1 have shown promising results in clinical trials. However, VP1 production remains costly because of expensive eukaryotic expression systems used for viral antigen synthesis. Many attempts to develop a bacterial strain producing vaccine-grade NoV VP1 failed. The aim of our study was to construct an Escherichia coli-based system to produce soluble VP1 of the predominant in Belarus NoV genovariants.
Methods: Expression vectors carrying genes encoding VP1 of NoV GI.3, GII.4, and GII.17 were created using Ligation Independent Cloning with pET42- and pColdI-based systems. The production level and solubility of target proteins were studied in E. coli ArcticExpress.
Results: Cold shock induction of recombinant VP1 genes combined with the pColdI vector and cold-adapted E. coli strain significantly increased the yield of full-length VP1 of NoV GI.3, GII.4, and GII.17 compared to pET42. The proteins were produced in soluble form, allowing particle assembly without a refolding step. The production level ranged from 10 to 99.8 mg per 1 liter of culture. All target proteins showed strong immunogenicity, important for generating NoV-specific antibodies and essential for vaccine development.
Conclusions/Learning Points: Our results suggest that these viral proteins can be used for NoV vaccine development and further studies on their antigenic properties.