Project Betanodavirus pathogenicity in farmed Senegalese sole (Solea senegalensis) and its relationship with the host immune response. Ministerio de Innovación y Competitividad (Spain), co-funded byFEDER (AGL2014-54532-C2)

Summary

Viral nervous necrosis (VNN) is a disease affecting a broad range of fish species worldwide, causing high mortalities, particularly in larval and juvenile stages. The ethiological agents of this disease are betanodaviruses, with a genome composed of two ssRNA molecules, RNA1, encoding the RNA-dependent RNA polymerase, and RNA2, encoding the coat protein. In addition, a subgenomic RNA, RNA3, is transcribed from the 3' end of the RNA1, and it encodes the B1 and B2 proteins. Betanodaviruses have been classified into four genotypes based on the T4 region within the RNA2 segment: SJNNV, TPNNV, BFNNV and RGNNV. However, in recent years it has been reported in Southern Europe the isolation of natural reassortants RG/SJ (RGNNV-type RNA1 and SJNNV-type RNA2). All these reassortants isolated from sole and gilthead sea bream in the Iberian Peninsula exhibited a slightly modified SJNNV capsid, with 3 different amino acid positions in all isolates, 2 of them affecting the C-terminal side of the coat protein, which is involved in host specificity and 1 in the N-terminal side. The residues located in the C-terminal side have previously been demonstrated to play a major role in virulence. The reassortants also show 19 amino acid substitutions in the polymerase compared to the RGNNV type. Finally in the non coding regions (UTR) of both genomic segments it was observed a mismatch of a total of 4 nucleotides with RG (RNA1) and SJ (RNA2) strains. These changes have been analyzed in this project and its role in virulence or in the replicacion capability has been demonstrated. However, it is well known that the course of the disease is not only due to the pathogen, but it is the result of the virus-host interaction, based on the stimulation of the immune system, which will be examined by the UMA research team. The viral infection induces both, the innate and the adaptative immune system. In order to characterize the induction of the immune system, the transcriptome masive sequencing (RNAseq) of the sole genome following the infection with betanodaviruses with different virulence to this fish species has been carried out. This approach has yielded valuable information on the main immunogenes involved in antiviral immune pathways and has been used for designing an OpenArrays based on Tagman real time PCR, which have been used to characterize the differential sole immune response after infections by betanodaviruses.

Research partners

Universidad de Málaga- Departamento de Microbiología

Universidade de Santiago de Compostela- Departamento de Microbiología y Parasitología-Instituto de Acuicultura

Publications

Souto S., Olveira J.G., Dopazo C.P., Borrego J.J., Bandín I. (2018) Modification of betanodavirus virulence by substitutions in the 3'terminal region of RNA2. J Gen Virol 99: 1210-1220 DOI 10.1099/jgv.0.001112 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6230769/)

Souto S., Olveira J.G., Vázquez Salgado L., Dopazo C.P., Bandín I. (2018) Betanodavirus infection in primary cultures from sole. Vet Res 49:8 DOI:10.1186/s13567-018-0580-4 (https://veterinaryresearch.biomedcentral.com/articles/10.1186/s13567-018-0580-4)

Souto S., Olveira J.G., Alonso M.C., Dopazo C.P., Bandín I (2018). Betanodavirus infection in bath challenged Solea senegalensis juveniles: A comparative analysis of RGNNV, SJNNV and reassortant strains. J. Fish Dis 41(10) DOI: 10.1111/jfd.12865

Souto, S., Olveira J.G., García-Rosado, Dopazo C.P., Bandín I (2018) Amino acid changes in the capsid protein of a reassortant betanodavirus strain: effect on viral replication in vitro and in vivo J. Fish Dis DOI: 10.1111/jfd.12916

Moreno P., Garcia-Rosado E., Borrego J.J., Alonso M.C. (2016) Genetic characterization and transcription analyses of the European sea bass (Dicentrarchus labrax) isg15 gene. Fish & Shellfish Immunology 55: 642-646. DOI 10.1016/j.fsi.2016.06.043.

Labella, AM Garcia-Rosado, E, Bandin, I, Dopazo, C P;Castro, D, Borrego, Juan J.J (2018) Transcriptomic Profiles of senegalese sole infected With nervous necrosis Virus reassortants Presenting Different Degree of Virulence. Frontiers in Immunology 9: 1626 DOI: 10.3389/fimmu.2018.01626 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6056728/)

Communications in Scientific Meetings

AM Podadera, D. Alvarez-Torres, S, Souto, E García-Rosado, I. Bandín & MC Alonso (2014) Differential stimulation of the type I Interferon system by different nodavirus genotypes in Senegalese sole *(Solea senegalensis)*. 9th International Symposium on Virus of Lower Vertebrates. Málaga

S Souto, J. G. Olveira, C. P. Dopazo & I. Bandín (2016) Estudio de vías de entrada y capacidad de replicación de diferentes genotipos de betnodavirus en lenguado. XI Congreso de Microbiología del Medio Acuático. Sociedad Española de Microbiología. Oviedo

S Souto, J. G. Olveira, C. López-Vázquez, J.J. Borrego, C. P. Dopazo & I. Bandín (2017). Amino acid changes in the capsid protein of a reassortant betanodavirus strain: effect on viral replication and in vivo in vitro. X International Symposium on virus in lower vertebrates (ISVLV) Budapest

S Souto, J. G. Olveira, C. López-Vázquez, L. Vázquez-Salgado, C. P. Dopazo & I. Bandín (2017) Primary neuron cultures from sole: a useful tool for betanodavirus infection studies. X International Symposium on virus in lower vertebrates (ISVLV) Budapest

A. Labella, J.J. Borrego, M. Manchado, I. Bandín, D. Castro, M.C. Alonso & E. García-Rosado (2017) Senegalese sole transcriptomic profiles in response to different betadonavirus RGNNV/SJNNV reassortant strains. X International Symposium on virus in lower vertebrates (ISVLV) Budapest