







AvBD11, the small protein found naturally in eggs that is packed with therapeutic potential

PRESS RELEASE: The chicken egg contains all the elements required for the development and protection of an embryo. It is a source of numerous molecules with various biological activities, although most of them still remain to be fully characterized. A consortium of scientists from INRAE, CNRS, Inserm and the University of Tours (1), investigated the structure and physiological functions of AvBD11, one of the major proteins of the chicken egg vitelline membrane (2). For the first time, the scientists have deciphered the unique properties of this small-size multifaceted protein, combining antimicrobial, anti-invasive (3) and cytotoxic activities. These results, published on December 23, 2019 in the Proceedings of the National Academy of Sciences of the United States of America, provide new insights into the role of egg proteins in embryonic development and on the specificities of the avian egg.



AvBD11 is a natural egg protein with considerable therapeutic potential © Christophe Maitre

The chicken egg contains about a hundred of molecules potentially involved in egg natural defense. These include antimicrobial peptides of the β -defensin family, such as the « avian β -defensin 11 » (AvBD11), which is uniquely found in the egg. A study previously published by one of the consortium partners demonstrated that this protein exhibits a broad antibacterial spectrum (4). Preliminary analyses of the protein sequence pointed out the atypical size of AvBD11 and the potential presence of two β -defensin-like domains (5), whereas all other avian β -defensins contains only one single domain.



Three-dimensional structure of AvBD11 determined by NMR (Centre de biophysique moléculaire, CNRS, Orléans, France)

The structural characterization of egg-purified AvBD11 by nuclear magnetic resonance (NMR) reveals that this protein has a compact structure consisting of two interacting β -defensin domains. This unique structural feature never described before, is proposed as the archetype of a new structural family called « avian double- β -defensins (Av-DBD) ». The two corresponding domains were individually obtained by chemical synthesis and their activities tested, alone or in synergy, to assess their respective contribution in the biological activity of native AvBD11. The results demonstrate that the antibacterial, antiparasitic and anti-invasive activities mainly rely on the first domain, while antiviral and cytotoxic activities are only observed for the whole protein, which underlines the pivotal and complementarity role of both domains for certain biological activities.

AvBD11 is a protein with multiple activities that are essential for the embryonic development of the bird, although it likely possesses other yet unknown functions. Besides its interest in developmental and evolutionary biology, such biological activities exhibited by AvBD11, could potentially be used in human health for the development of polyvalent therapeutic agents targeting infectious diseases but also cell disorders associated with cancer (patent application pending). This work is one example of getting inspired by natural molecules that have been shaped during evolution and "time-felt" to protect the avian embryo, to develop new efficient therapeuticals.

1 This work was conducted as part of two research projects financed by Région Centre-Val de Loire: « MUSE » (Medicinal USe of Eggs », 2014-00094512) coordinated by S. Réhault-Godbert, and « SAPhyR-11 » (Structure/Activity and PHYlogenetic Relationships of AvBD11, 2017-119983) coordinated by N. Guyot. The MUSE project was dealing with structural and functional characterization of peptides and proteins purified from egg and with the assessment of their potential value in human and animal Health. This project allowed the identification of a promising peptide, AvBD11, which was further characterized in the SAPhyR-11 project. 2 Proteinaceous layer surrounding the egg yolk

3 Inhibitory activity of cell migration (within a matrix substrate) allowing a control of the dissemination of cells within a tissue or an organism

4 Purification and characterization of avian beta-defensin 11, an antimicrobial peptide of the hen egg. Hervé-Grépinet et al. Antimicrob Agents Chemother doi: 10.1128/AAC.00204-10. 5 Part of a protein forming a basic structural and functional unit

References

Structure, function and evolution of Gga-AvBD11, the archetype of a new structural avian-double-β-defensin family, Guyot *et al.,* Proceedings of the National Academy of Sciences, <u>doi: 10.1073/pnas.1912941117</u>

Patent application FR18 57411 of 9/08/2018 and PCT/EP2019/071388 « PEPTIDES DERIVES D'UNE BETA-DEFENSINE 11 AVIAIRE ET LEURS UTILISATIONS » (Peptides derived from an avian beta-defensin 11 and their applications)

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