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The *Xenopus* Oocyte: A Tool for Membrane Biology

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The *Xenopus* is a special study model in experimental research. In embryology, it has been used to understand the harmonious development of a complex organism from its fertilized cell. In toxicology, it is the model of choice for observing the deleterious effects of endocrine disruptors. In pharmacology, female oocytes have been used for over forty years to express genes of interest. In fact, the membrane of *Xenopus* oocytes is relatively poor in membrane receptors and ion channels. Furthermore, these cells are relatively large (1–2 mm), making it easy to express proteins by injecting DNA or RNA, or by transplanting membranes using a xenograft protocol. These techniques have enabled scientists to characterize receptors and transporters outside their physiological context.

Our Special Issue, entitled “The *Xenopus* Oocyte: A Tool for Membrane Biology” in the journal *Membranes*, aimed to give this cell, which is widely utilized by researchers working on membrane proteins, the place it deserves in our time. Most of the articles that are published in this issue use the oocyte as an expression system, i.e., a cell in which we express or overexpress a protein whose normal or altered functioning we wish to understand. Indeed, the heterologous expression of membrane receptors is indispensable for understanding the changes, particularly electrophysiological, that are induced by mutations in the corresponding gene or through their targeting with pharmacologically active molecules.

The expression of various receptors and ion channels therefore constitutes most of the papers published in this Special Issue. Using a classical electrophysiology approach based on two-electrode voltage clamp recording, Bertaud et al. [1] compared the effect of several widely used insecticides on human and insect GABA receptors. The use of the *Xenopus* oocyte is underlined by the pharmacological differences that exist between these GABA receptors in their differential sensitivity to insecticides. Rousset et al. [2] have adapted the membrane transplantation method that was developed in the 1990s by Miledi [3] to characterize the electrophysiological properties of voltage-gated Ca²⁺ channels from micro-transplanted mouse tissues. This original method could eventually serve as a screening platform for channelopathies. The same approach has been used by Miller et al. [4] to characterize the currents that are linked to the activation of metabotropic glutamate receptors (mGluRs): the microtransplantation of synaptosome membranes from rat cortexes facilitates the study of their properties. In a detailed review, Ivorra et al. recall the principle of this membrane transplantation, as well as the advantages and disadvantages associated with this original methodology, initiated with Torpedo electroplates and subsequently extended to all types of mammalian and even invertebrate tissues [5–8].

Numerous membrane receptors can be expressed in the *Xenopus* oocyte to characterize their biophysical or pharmacological properties using the two-electrode voltage clamp technique. In a study by Isaev et al. [9], the antagonistic effect of methylene blue on K_{ATP} channels was demonstrated by measuring the intensity of a current induced by cromakalim. And Cav2.1 channel variants causing ataxic channelopathies revealed electrophysiological gains or losses of function in the study by Folacci et al. [10]; the molecular modelling of these mutations or of the associated neuronal excitability confirms the electrophysiological



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findings. Lummis and Dougherty explored the contribution of proline residues on $\alpha 1$ subunit glycinergic receptors to their sensitivity to glycine. By generating substitution point mutations, they demonstrated the functional importance of Pro residues [11]. Finally, Stein et al. used the oocyte to express tight junction proteins in a two-cell model [12]. Their data show that the activity of claudin proteins is largely pH-dependent.

However, far from being just an expression system, the *Xenopus* oocyte can also be used as a cell for the development of innovative membrane protein monitoring techniques. Thus, by coupling the measurement of voltage-gated Na^+ and K^+ currents with the optogenetic photosensitivity of channelrhodopsin, vom Dahl et al. [13] could observe and measure the characteristics of action potentials that were specific to excitable cells. Their work could lead to the development of a genuine pharmacological platform for testing therapeutic compounds and assessing the impact of genetic mutations on cell excitability. Some studies have focused on membrane targets that are endogenously expressed in the *Xenopus* oocyte. For example, Bernareggi et al. [14] investigated endogenous Cl^- currents (TMEM16A Ca^{2+} -activated chloride channels). This study shows that a compound that is present in asbestos fibers, crocidolite, induces an indirect activation of these channels via an increase in intracellular Ca^{2+} , shedding further light on the carcinogenic effects of asbestos.

In conclusion, the use of this very special cell, the *Xenopus* oocyte, has enabled numerous scientific teams to work on a considerable variety of receptors and transporters, approaching them from biophysical, pharmacological, biochemical, electrophysiological and toxicological angles, among others [15]. A number of studies that utilize this cell have been cited hundreds of thousands of times, highlighting its versatility and adaptability for the expression of any type of receptor [16]. It is a very convenient link between molecular expression work and its physiological or pathophysiological extensions. As Gamba points out, many fields of physiology, such as arterial blood pressure, neuronal excitability, mineral metabolism and cell volume regulation, are initiated using the *Xenopus* oocyte [17]. Easy to obtain and use, the *Xenopus* oocyte is a very practical system in the toolbox of scientists who wish to have a cellular model for expressing genes of interest.

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References

- Bertaud, A.; Cens, T.; Mary, R.; Rousset, M.; Arel, E.; Thibaud, J.B.; Vignes, M.; Ménard, C.; Dutertre, S.; Collet, C.; et al. *Xenopus* Oocytes: A Tool to Decipher Molecular Specificity of Insecticides towards Mammalian and Insect GABA-A Receptors. *Membranes* **2022**, *12*, 440. [[CrossRef](#)] [[PubMed](#)]
- Rousset, M.; Humez, S.; Laurent, C.; Buée, L.; Blum, D.; Cens, T.; Vignes, M.; Charnet, P. Mammalian Brain Ca^{2+} Channel Activity Transplanted into *Xenopus laevis* Oocytes. *Membranes* **2022**, *12*, 496. [[CrossRef](#)] [[PubMed](#)]
- Marsal, J.; Tigyi, G.; Miledi, R. Incorporation of acetylcholine receptors and Cl^- channels in *Xenopus* oocytes injected with *Torpedo* electroplaque membranes. *Proc. Natl. Acad. Sci. USA* **1995**, *92*, 5224–5228. [[CrossRef](#)] [[PubMed](#)]
- Miller, B.; Moreno, N.; Gutierrez, B.A.; Limon, A. Microtransplantation of Postmortem Native Synaptic mGluRs Receptors into *Xenopus* Oocytes for Their Functional Analysis. *Membranes* **2022**, *12*, 931. [[CrossRef](#)] [[PubMed](#)]
- Ivorra, I.; Alberola-Die, A.; Cobo, R.; González-Ros, J.M.; Morales, A. *Xenopus* Oocytes as a Powerful Cellular Model to Study Foreign Fully-Processed Membrane Proteins. *Membranes* **2022**, *12*, 986. [[CrossRef](#)] [[PubMed](#)]
- Miledi, R.; Eusebi, F.; Martínez-Torres, A.; Palma, E.; Trettel, F. Expression of functional neurotransmitter receptors in *Xenopus* oocytes after injection of human brain membranes. *Proc. Natl. Acad. Sci. USA* **2002**, *99*, 13238–13242. [[CrossRef](#)] [[PubMed](#)]
- Palma, E.; Reyes-Ruiz, J.M.; Lopercolo, D.; Roseti, C.; Bertollini, C.; Ruffolo, G.; Cifelli, P.; Onesti, E.; Limatola, C.; Miledi, R.; et al. Acetylcholine receptors from human muscle as pharmacological targets for ALS therapy. *Proc. Natl. Acad. Sci. USA* **2016**, *113*, 3060–3065. [[CrossRef](#)] [[PubMed](#)]
- Crespin, L.; Legros, C.; List, O.; Tricoire-Leignel, H.; Mattei, C. Injection of insect membrane in *Xenopus* oocyte: An original method for the pharmacological characterization of neonicotinoid insecticides. *J. Pharmacol. Toxicol. Methods* **2016**, *77*, 10–16. [[CrossRef](#)] [[PubMed](#)]
- Isaev, D.; Yang, K.S.; Petroianu, G.; Lorke, D.E.; Oz, M. Methylene Blue Inhibits Cromakalim-Activated K^+ Currents in Follicle-Enclosed Oocytes. *Membranes* **2023**, *13*, 121. [[CrossRef](#)] [[PubMed](#)]

10. Folacci, M.; Estaran, S.; Ménard, C.; Bertaud, A.; Rousset, M.; Roussel, J.; Thibaud, J.B.; Vignes, M.; Chavanieu, A.; Charnet, P.; et al. Functional Characterization of Four Known Cav2.1 Variants Associated with Neurodevelopmental Disorders. *Membranes* **2023**, *13*, 96. [[CrossRef](#)] [[PubMed](#)]
11. Lummis, S.C.R.; Dougherty, D.A. Expression of Mutant Glycine Receptors in *Xenopus* Oocytes Using Canonical and Non-Canonical Amino Acids Reveals Distinct Roles of Conserved Proline Residues. *Membranes* **2022**, *12*, 1012. [[CrossRef](#)] [[PubMed](#)]
12. Stein, L.; Brunner, N.; Amasheh, S. Functional Analysis of Gastric Tight Junction Proteins in *Xenopus laevis* Oocytes. *Membranes* **2022**, *12*, 731. [[CrossRef](#)] [[PubMed](#)]
13. Vom Dahl, C.; Müller, C.E.; Berisha, X.; Nagel, G.; Zimmer, T. Coupling the Cardiac Voltage-Gated Sodium Channel to Channelrhodopsin-2 Generates Novel Optical Switches for Action Potential Studies. *Membranes* **2022**, *12*, 907. [[CrossRef](#)] [[PubMed](#)]
14. Bernareggi, A.; Zangari, M.; Constanti, A.; Zacchi, P.; Borelli, V.; Mangogna, A.; Lorenzon, P.; Zabucchi, G. Asbestos Fibers Enhance the TMEM16A Channel Activity in *Xenopus* Oocytes. *Membranes* **2023**, *13*, 180. [[CrossRef](#)] [[PubMed](#)]
15. Bhatt, M.; Di Iacovo, A.; Romanazzi, T.; Roseti, C.; Cinquetti, R.; Bossi, E. The “www” of *Xenopus laevis* Oocytes: The Why, When, What of *Xenopus laevis* Oocytes in Membrane Transporters Research. *Membranes* **2022**, *12*, 927. [[CrossRef](#)] [[PubMed](#)]
16. Caterina, M.J.; Schumacher, M.A.; Tominaga, M.; Rosen, T.A.; Levine, J.D.; Julius, D. The capsaicin receptor: A heat-activated ion channel in the pain pathway. *Nature* **1997**, *389*, 816–824. [[CrossRef](#)] [[PubMed](#)]
17. Gamba, G. Arterial Blood Pressure, Neuronal Excitability, Mineral Metabolism and Cell Volume Regulation Mechanisms Revealed by *Xenopus laevis* oocytes. *Membranes* **2022**, *12*, 911. [[CrossRef](#)] [[PubMed](#)]

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