

# medicina

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differences are observed between both populations and pure DPPC. The most noticeable changes were observed at the methylenes groups at different RH indicating that water between aliphatic chains (confined water) remain at low hydration degrees in the presence of high concentrations of both aminoacids. A similar behavior in the water content and confined water was observed in ETERPC MLV' s.

These results gave suggest that the aminoacids enhance the water entrapment in the membrane, a response that may be helpful to interpret their preservative properties in hydric stress process.

**Keywords:** Liposomes, Hydration, FTIR-ATR, Aminoacids.

**(339) PLASMA MEMBRANE POTENTIAL (PM<sub>v</sub>) AND ITS ROLE IN THE RECRUITMENT OF CYTOSOLIC PROTEINS TO THE PLASMA MEMBRANE**

Melisa Balach, Verónica Santander, Cesar Casale, Alexis Campetelli

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Previously, our group showed that erythrocytes from diabetic and hypertensive patients displayed more tubulin associated with the plasma membrane than erythrocytes from normal subjects. This association results in the inhibition of plasma membrane P-ATPases, as Na<sup>+</sup>,K<sup>+</sup>-ATPase and Ca<sup>2+</sup>-ATPase. Consequently, the intracellular concentrations of Na<sup>+</sup> and Ca<sup>2+</sup> increases and it has been established a relationship between the content of membrane tubulin, the changes in the intracellular concentration of some ions and the alteration of some hemorheological properties of these cells, as deformability and osmotic fragility. Since the PM<sub>v</sub> is generated as a result of the distribution of electrical charges on both sides of the membrane, the inhibition of ionic pumps could affect the PM<sub>v</sub>. Given some physicochemical properties of tubulin, and using biochemical tools and the electric-sensitive fluorescent dye DiBAC<sub>4</sub>(3) we designed experiments to know whether changes in the PM<sub>v</sub> could influence the migration of tubulin to the plasma membrane. For this purpose, we modified pharmacologically the PM<sub>v</sub> in erythrocytes from healthy individuals, and then we quantified tubulin in isolated plasma membranes. We observed a marked increase in membrane tubulin in erythrocytes that were depolarized, whereas in hyperpolarized erythrocytes, the amount of tubulin in membrane was relatively minor and was mostly of the acetylated isotype. On the other hand, and using flow cytometry and DiBAC<sub>4</sub>(3), we determined the PM<sub>v</sub> in erythrocytes from spontaneously hypertensive rats (strain SHR) and control mates (Wistar Kyoto strain). The results showed that erythrocytes from SHR rats displayed a 17% higher fluorescence compared with control animals (which theoretically represents a variation of around 2 mV), suggesting that this erythrocytes are depolarized when compared whit normal erythrocytes. These results suggest that there exists a relationship between PM<sub>v</sub> and the association of tubulin to the plasma membrane.

**Keywords:** tubulin, membrane potential, erythrocyte.

**(1415) ALLOSTERIC ACTIVATION OF THE HUMAN 5-HT<sub>3</sub> RECEPTOR**

Camila Fabiani, Noelia Redríguez-Araujo, Cecilia Bouzat, Jeremías Corradi

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The serotonin type 3 receptors (5-HT<sub>3</sub>) are cation-selective channels that belong to the Cys-loop receptor family. They are involved in fast excitatory transmission in central and peripheral nervous systems and are implicated in gastrointestinal and neurological functions. Five different subunits (A-E) have been identified in humans, and the A subunit is the only one capable of forming functional homopentameric receptors (5-HT<sub>3</sub>A). These receptors are activated by agonist binding to the orthosteric sites located at the interfaces between two adjacent subunits at the extracellular region. Ago-positive allosteric modulators (Ago-PAMs) are ligands that bind to an allosteric binding site and mediate a receptor response in the absence of an orthosteric agonist and also potentiate its response. We here used the high-conductance form of the receptor (5-HT<sub>3</sub>A<sub>HC</sub>), which allows detection of single-channel openings from patch-clamp

recordings, to determine the molecular basis underlying its activation and modulation by two ago-PAMs, thymol and carvacrol. From cell-attached recordings, we observed that both ligands activate the receptor in a similar way, eliciting openings in quick succession that are grouped in episodes (bursts) of high open probability (>0.9). The combined application of orthosteric agonists (full or partial) with the allosteric ligands elicits single channel events whose mean open and burst durations are intermediate between those obtained when orthosteric or allosteric agonists are applied individually.

Our results reveal the mechanistic basis underlying activation and modulation of the 5-HT<sub>3</sub>A receptor by two ago-positive allosteric modulators, thus providing new information that is essential for the design of more efficacious and specific therapeutic compounds.

**Keywords:** serotonin, positive allosteric modulators, single-channel.

**(576) CONTRIBUTION OF ACCESSORY SUBUNITS TO HETEROMERIC SEROTONIN TYPE 3 RECEPTOR FUNCTION**

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**Abstract:** 5HT<sub>3</sub> receptors are members of the Cys-loop receptor family that mediate fast excitatory transmission in central and peripheral nervous system. Five different subunits (AE) have been identified in humans, and most of them have multiple isoforms. It is known that the A subunit can form functional homomeric (5HT<sub>3</sub>A) and heteromeric receptors with the B subunit (5HT<sub>3</sub>AB). Here we combined single-channel and macroscopic current recordings to determine if the other 5HT<sub>3</sub> subunits (C, D or E) can also combine with the A subunit to form heteromeric receptors. After co-expression of the A subunit with each of the tested subunits, single-channel events with different amplitudes to that of 5HT<sub>3</sub>A receptors were detected. From the analysis of the single-channel amplitudes, the stoichiometry of each heteromeric receptor was inferred. The activation patterns of the heteromeric receptors elicited by 1030 μM 5HT showed long-activation episodes composed by openings in quick succession. No statistically significant differences in the open durations were observed among the homomeric and the heteromeric A/C, A/D, A/E receptors. However, the EC<sub>50</sub> values for 5HT, which were determined by whole-cell macroscopic recordings, were statistically different between heteromeric and 5HT<sub>3</sub>A receptors. *In silico* studies provided insights into the contribution of the different subunits to the 5HT binding site.

Our results demonstrate that all the 5HT<sub>3</sub> subunits can combine with the A subunit to form heteromeric receptors, thus leading to a wide variety of receptors showing different functional properties. The functional characterization of different heteromeric 5HT<sub>3</sub> receptors, which are expressed in different tissues, contributes to the development of selective therapies targeting this receptor family.

**Keywords:** serotonin, single-channel, heteromeric receptors.

**STRUCTURAL AND FUNCTIONAL BIOCHEMISTRY 6**

**(137) ACIDIC PH IS A SIGNAL THAT TRIGGERS THE PHOSPHORYLATION OF THE RESPONSE REGULATOR NTRX IN ALPHAPROTEOBACTERIA**

Ignacio Fernandez, Gabriela Sycz, Fernando Goldbaum, Mariela Carrica

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*Caulobacter crescentus* is a gram-negative bacterium that grows in dilute aquatic environments and is a member of the alpha-subdivision of proteobacteria. Much attention has been given to the study of *C. crescentus* signaling pathways to describe how they control cellular development and cell-cycle progression. A system-level study of two-component systems (TCS) described that the gene that codes for the response regulator (RR) NtrX was conditionally essential because it was only possible to obtain a deletion strain of this gene in a minimal medium. However, the signal to which NtrX responds and its role in *C. crescentus* biology remains elusive. On