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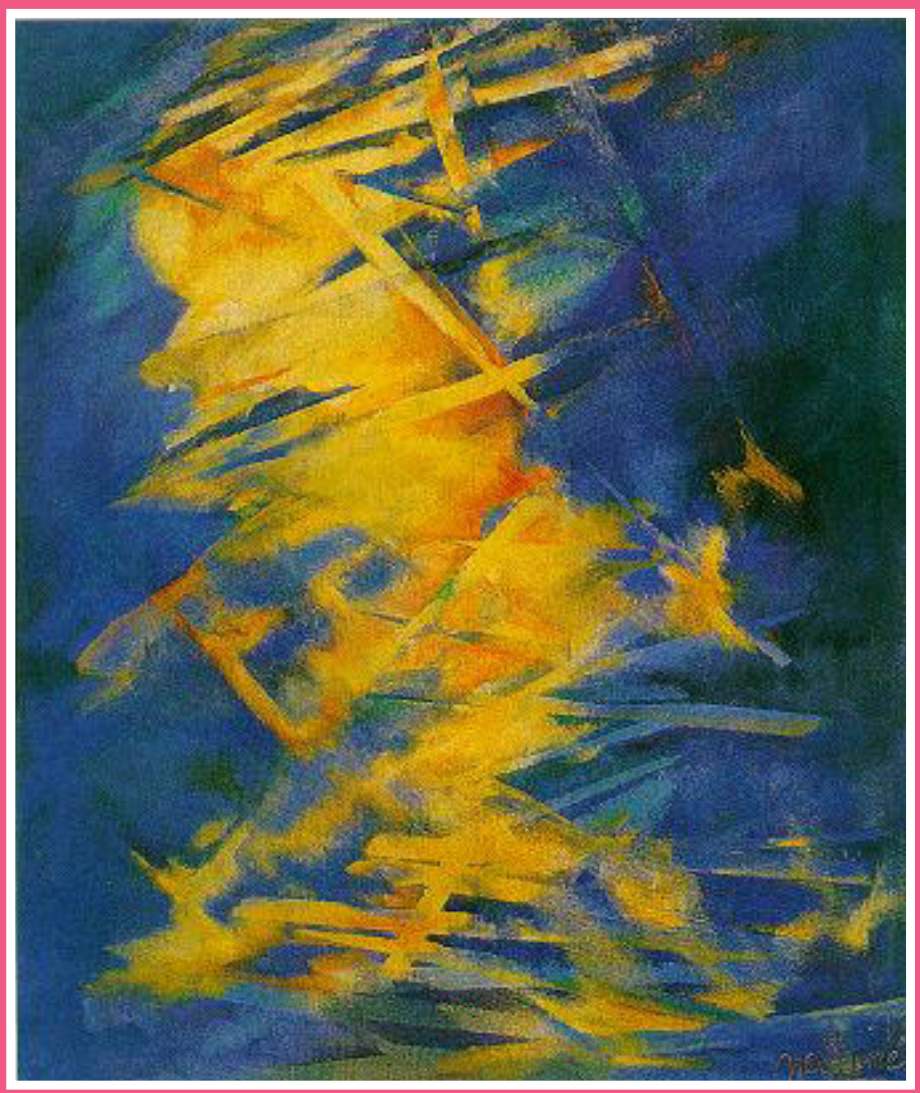

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and control mates (Wistar Kyoto strain). The results showed than erythrocytes from SHR rats displayed a 17% higher fluorescence compared with control animals (which theoretically represents a variation of around 2 mV), suggesting than this erythrocytes are depolarized when compared whit normal erythrocytes. These results suggest that there exists a relationship between PM_V and the association of tubulin to the plasma membrane.

Keywords: tubulin, membrane potential, erythrocyte.

(1415) **ALLOSTERIC ACTIVATION OF THE HUMAN 5-HT$_3$ RECEPTOR**

Camila Fabiani, Noelia Redriguez Araujo, Cecilia Bouzat, Jeremías Corradi
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The serotonin type 3 receptors (5-HT$_3$) 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$_3$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$_3$A$_{HC}$), 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$_3$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$_3$ 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$_3$A) and heteromeric receptors with the B subunit (5HT$_3$AB). Here we combined single-channel and macroscopic current recordings to determine if the other 5HT$_3$ 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$_3$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_{50} values for 5HT, which were determined by whole-cell macroscopic recordings, were statistically different between heteromeric and 5HT$_3$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$_3$ 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$_3$ receptors, which are expressed in different tissues, contributes to the development of selective therapies targeting this receptor family.

Keywords: serotonin, single-channel, heteromeric receptors.

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(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
Fundación Instituto Leloir, IIBBA-CONICET

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 the other hand, NtrX and its cognate histidine kinase NtrY have been extensively studied in the pathogen *Brucella abortus*, where it has been reported that they participate in the bacterial adaptation to low oxygen tension.

Here, we show conditions required for NtrX expression in *C. crescentus*, as well as a signal that triggers NtrX phosphorylation, and we describe the relevant role of this RR during growth in minimal media. We found that NtrX expression is induced by high concentrations of phosphate, despite the fact that the system does not respond to it. Instead, we demonstrate that acidic pH leads to NtrX phosphorylation and that this signal is physiologically relevant because *C. crescentus* produces the acidification of the medium upon entry to stationary phase, causing NtrX phosphorylation at this stage of the growth curve. Besides, we show that *ntrX* deletion produces a decreased viability at stationary phase and a reduced resistance to acidic stress. Finally, we prove that NtrX is also phosphorylated by acidic pH in *B. abortus*, pointing out to a potential conserved role across the alphaproteobacteria class.

Keywords: NtrY/X two component system, Caulobacter crescentus, Brucella abortus, acidic pH sensing

(289) **STRUCTURAL ANALYSIS OF THE BLUE LIGHT PHOTORECEPTOR FROM *BRUCELLA***

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Fundación Instituto Leloir - IIBBA CONICET

Light modulates the virulence of the bacterium *Brucella abortus* through a histidine kinase containing a light-oxygen-voltage domain sensitive to blue light (LOV-HK). *Brucella* LOV-HK exhibits the spectroscopic changes corresponding to the typical adduct formation of LOV domains, between the C4 of the isoalloxazine ring and S of a strictly conserved cysteine. After illumination, *Brucella* LOV-HK does not return to the dark state. *Brucella* LOV-HK increases its autophosphorylation upon absorption of blue light.

Brucella LOV-HK comprises an N-terminal blue-light sensor (LOV) domain, followed by a central PAS domain and a C-terminal histidine kinase (HK) domain. We have performed a structural characterization of the isolated LOV and HK domains.

The LOV domain consists of a globular core and N- and C-terminal flanking regions. The core of the LOV domain adopts the typical α/β PAS domain fold, consisting of a β-sheet and α-helical connector