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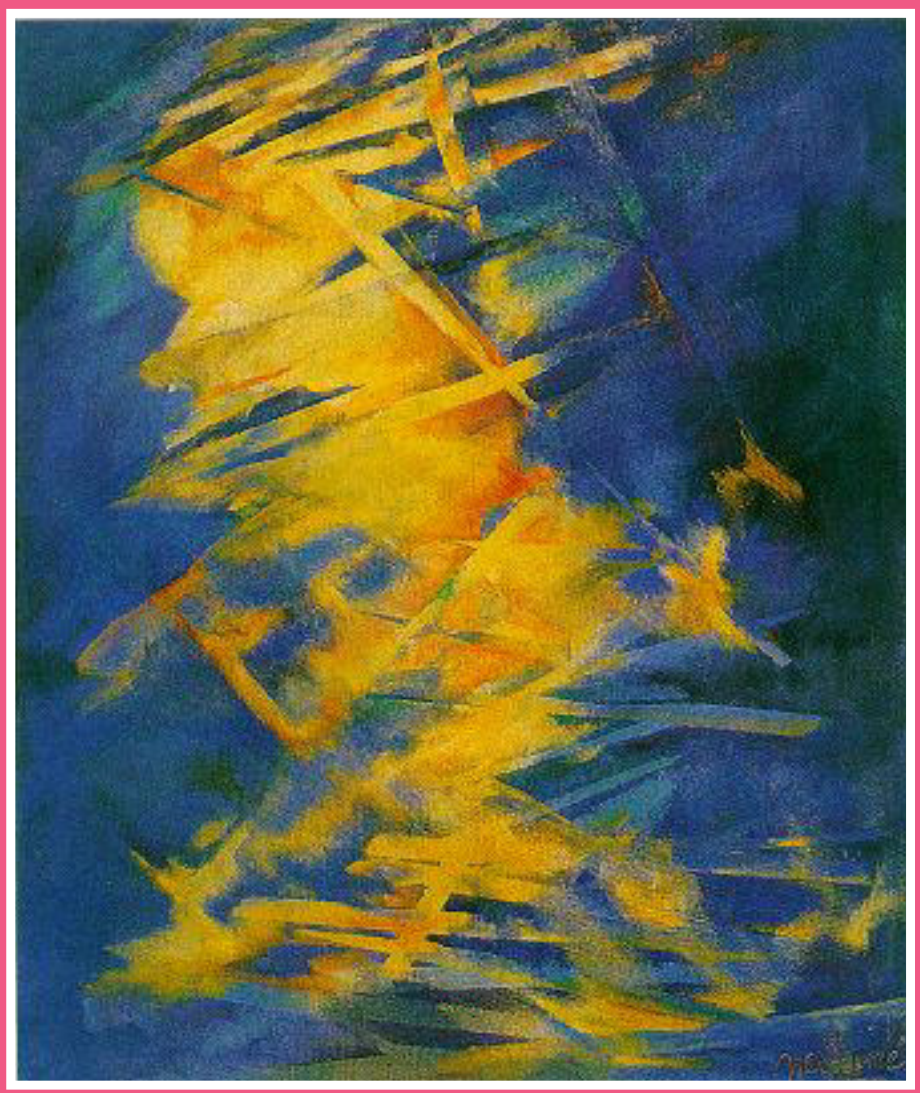

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observed but not with lysozyme. The results confirm the specific interaction of AzRu with calcium dependent proteins. Photolabeling mass spectra of PMCA with AzRu showed the disappearance of signals from certain peptides from the cytoplasmic domains suggesting an interaction with AzRu. Due to the difficulty of studying membrane proteins by mass spectrometry, we are evaluating an optimization of the study of the transmembrane domain where the PMCA-AzRu adduct would be found.

Keywords: Plasma Membrane Calcium ATPase, Azido-Ruthenium reagent, Ca^{2+} binding site, mass spectrometry

(692) **STUDY OF THE MECHANICAL GATING OF THE AQUAPORIN FAPIP2;1 FROM STRAWBERRY**

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Recently, we published the first works that experimentally demonstrate the direct regulation of both plant and animal aquaporins by membrane tension (s) changes. Our recent work with *Bv*TIP1;2 and *Bv*PIP2;1 from red beet show that the first one is mechanosentive while the second one is not. This different behavior could be related to the differential distribution of GxxxG sequences (suggested to be responsible for mechanosensitivity in ion channels) observed by homology modeling. Previously we demonstrated that hAQP1 is a mechanosensitive channel. Both the water permeability (P_f) and the elastic volumetric coefficient (*E*) are negatively correlated in experiments with hAQP1 and *Bv*TIP1;2 (R^2>0.98), indicating that these aquaporins close with s increments. Phylogenetics analysis indicate that AQP1 and PIPs share a common ancestor and that divergence of the AQP1-PIP and TIPs groups occurred earlier in evolution. Therefore, three hypotheses arise for mechanosensitivity: 1) it would had been present in the ancestor of AQP1-PIPs and TIPs and was lost in PIPs; 2) it appeared in AQP1-PIPs and TIPs by separately; 3) *Bv*PIP2;1 is a mechanosensitive channel but less sensitive than hAQP1 and *Bv*TIP1;2. Now, we are studying the mechanosensitive properties of *Fa*PIP2;1 from strawberry. The homology model of *Fa*PIP2;1 shows differences with *Bv*PIP2;1 and similarities with *Bv*TIP1;2, suggesting that *Fa*PIP2;1 could behave as a mechanosensitive aquaporin. By means of simultaneous V and P measurements in Xenopus oocytes expressing *Fa*PIP2;1 we determine P_f and *E* under osmotic gradients. Our previous results with osmotic gradients up to 200 mOmol.Kg_{H2O}^{-1} (E=0.5-0.8 KPa) showed that *Bv*PIP2;1 is not regulated by membrane tension changes. Preliminary results with *Fa*PIP2;1 show that this aquaporin does not behave as a mechanosenstive channel, at least up to changes induced with 200 mOmol.Kg_{H2O}^{-1}.

Keywords: water permeability; aquaporin; PIP; membrane tension; volumetric elastic modulus

(1757) **AMYLOID β PEPTIDE DECREASES α7 RECEPTOR POTENTIATION**

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Amyloid β peptide (Aβ) is a key player in the development of Alzheimer disease (AD). Aβ is visible as the primary component of senile plaques in the brains of Alzheimer's patients. Cholinergic activity mediated by human α7 nicotinic receptors is decreased in AD, and potentiation of α7 by positive allosteric modulators (PAMs) is emerging as a novel therapeutic strategy for improving memory and cognition. There are reports showing functional interaction of Aβ with α7, but the reported effects are very varied and the underlying mechanisms are not clear. Here we explored the effect of Aβ1-40 and Aβ1-42 on human α7 at the patch-clamp single-channel level. α7 channel activity elicited by 100 μM ACh consists of brief and isolated openings. In the presence of PAMs, open channel lifetime is increased and openings appear grouped in long activation episodes. The type II PAM PNU-120596 (1 μM) prolongs open durations and elicits activation episodes of ~2 s. In the presence of Aβ there is a statistically significant decrease in the mean duration of the potentiated activation episodes, which is 2.6-fold at 100 nM Aβ1-40 ($p<0.001$, n=11) and 2-fold at 100 nM Aβ1-42 ($p<0.05$, n=10). To determine if the effect is specific for PNU-120596, we also tested NS-1738, which is an α7 type I PAM. Again, a 2-fold reduction in the duration of the activation episodes is observed ($p<0.001$). Complementary fluorescence spectroscopic studies using a fluorescent channel blocker, crystal violet, that binds with different affinities to resting and desensitized receptors provide insights into the functional changes. Our results demonstrate that Aβ inhibits potentiation of human α7, probably through an allosteric mechanism which involves slow block or increased desensitization. Deciphering the functional interaction between α7 and Aβ contributes to the understanding of the involvement of α7 in the pathophysiology of Alzheimer disease.

Keywords: Amyloid β peptide, nicotinic receptor, Patch-clamp, ion channel

(547) **ALL YOU NEED IS COFFEE**

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Cholinergic deficit is regarded as an important factor responsible for Alzheimer's disease symptoms. Two molecular targets for the treatment of this disease are acetylcholinesterase (AChE) and nicotinic receptor (nAChR). Caffeine (CAFF) acts as a non-competitive inhibitor of AChE but its mechanism of action on nAChR is still unknown. To this end, we first explored if CAFF influences the nAChR conformational state using the AChR conformational-sensitive probe crystal violet (CrV) and AChR-rich membranes from *T. californica*. CAFF induced changes in the KD value of CrV in a concentration-dependent manner taking the nAChR to a state close to the desensitized one. In the presence of α-bungarotoxin, a specific nAChR competitive antagonist, high concentrations of CAFF increased the KD value of CrV, compatible with a competition for the CrV site in the channel pore. The same effect was seen with galantamine, an AChE inhibitor and partial agonist of nAChR. To understand the molecular mechanism underlying the conformational changes of the nAChR, we expressed adult muscle or neuronal a7 nAChRs in BOSC cells, and performed single channel recordings with different CAFF concentrations in the presence or absence of ACh. At low concentrations (1-300 μM), CAFF activated muscle and a7 nAChRs, and the activation profile was independent of CAFF concentration. On the other hand, at high CAFF concentrations (up to 20 mM), the mean open duration decreased, the relative area of the briefer closed component and the cluster duration increased, and a flickering behavior was observed, these suggesting that CAFF acts as an open channel blocker. Thus, we here demonstrate a dual effect of CAFF on muscle and a7 nAChRs, behaving as a weak agonist at low concentrations and as a negative modulator at high concentrations. Our results bring new information about the mechanism of modulation of pharmacology targets for the design of new therapies for the intervention in neurological diseases.

Key words: Caffeine, nicotinic receptor, crystal violet, single channel recordings.

STRUCTURAL AND FUNCTIONAL BIOCHEMISTRY 2

(224) **CHARACTERIZATION OF THE CHDL DOMAINS OF RapA, AN EXTRACELLULAR LECTIN FROM *Rhizobium leguminosarum* INVOLVED IN BIOFILM MATRIX ASSEMBLY**

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Abstract: In natural environments microbes live in multicellular structures called biofilms, in which cells are embedded in a matrix of self-produced biopolymers. The extracellular matrix determines the immediate conditions of life of biofilm cells, and also provides adhe-