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Identification of GABA receptor genes and evidence of GABA signaling during embryogenesis of the sea urchin

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Gamma-aminobutyric acid (GABA) is the principal inhibitory neurotransmitter in the mammalian central nervous system and acts via ionotropic ($GABA_A$-R_s) and metabotropic ($GABA_B$-R_s) receptors. $GABA_A$-R_s are Cl^- selective hetero-pentameric channels assembled by combinations of 19 distinct gene products. Instead, $GABA_B$-R_s are bi-subunit G-protein coupled receptors linked to K^+ or Ca^{2+} channels. Dysfunctions of GABA-signaling (GS) cause psychotic disorders and correlate with epigenetic alterations, such as over-expression of DNA methyl transferase-1 which in turn imposes iper-methylation of GABA-regulated genes. The sea urchin embryo, which presents a rudimentary nervous system, offers a big opportunity to study the GS and its potential epigenetic implications in a simple eukaryote model. To this purpose, we performed a comprehensive *in silico* analysis of the sea urchin genome and identified a 450 Kb long cluster containing two genes encoding for the $GABA_B$-R subunits, and two genes respectively encoding for a α/γ/ε-type and a β/ρ/δ/τ/π-type $GABA_A$-R subunit. From an evolutionary perspective, this result revealed a unique genomic organization of these genes in sea urchin. Next, to preliminarily evaluate the role of GS during development, *Paracentrotus lividus* embryos were cultured in the presence of GABA at concentrations ranging from 0.01 to 1.0 mM. Compared to controls, treated embryos showed aberrations in axial patterning, with a dose-dependent effect. In particular, at 48 hours post-fertilization control embryos were normal bilateral symmetric plutei whereas GABA-treated embryos displayed a radial organization with supranumerary spicules. Washout experiments allowed to determine that the period of sensitivity is restricted from the blastula to the gastrula stage. Altogether, these results suggest that dysregulation of GS affects the polarization of the ectoderm. Although preliminary, this study provide the first evidence of GS activity during development of echinoderms.