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Enhancement of Odor Avoidance
Regulated by Dopamine Signaling in Caenorhabditis Elegans

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The Journal of Neuroscience, 30, 16365-16375 (2010)

Transition from Positive to Neutral in Mutation Fixation along with Continuous Rising Fitness in Thermal Adaptive Evolution

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PLoS Genetics, 6, e1001164 (2010)

CD3 is a Therapeutic Target in Human Liver Cancer Stem Cells

(Graduate School of Medicine)

The Journal of Clinical Investigation, 129(9), 3326-3339 (2010)

Environmental Sex Determination in the Branchiopod Crustacean Daphnia magna: Deep Conservation of a Doublesex Gene in the Sex-determining Pathway

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The Journal of Neuroscience, 30, 16365-16375 (2010)

Cancer stem cells (CSCs) are involved in resistance to chemo-radiation therapy and occurrence of tumor relapse and progression. We demonstrate that CD3+ cells act as potent dormant CSCs in human liver cancer, and thus, suggest a novel approach for treating liver cancer based on CSC concepts. CD3+ cells exhibit a prolonged dye-retaining capacity, high resistance to anti-cancer drugs and irradiation. CD3 regulates reactive oxygen species (ROS) scavenger, elicits a reduction in ROS-induced DNA damage after genotoxic chemo-radiation stress, and protects cells from apoptosis. In mouse models, combination with a CD3 inhibitor and free radical inducible chemo-radiation drastically reduced tumor volume and inhibited self-renewal activity of CSCs.

The authors have found a highly significant connection between the evolution of various mechanisms underlying protochlorophyllide reductase 4 in vivo, which remains unclear. We studied dopamine-dependent neural function in the nematode C. elegans as a model for genetic analysis of in vivo dopamine signaling. We found that odor avoidance behavior of C. elegans is enhanced after preexposure to the odor, and that the enhancement requires dopamine signaling via a D2-like dopamine receptor in a pair of interneurons. Moreover, D2-type dopamine receptor antagonists, such as the antipsychotic drug haloperidol, specifically suppressed similarity to dox gene, which plays a critical role in controlling sex differentiation in genetic sex determination such as vertebrates.

The identified gene showed higher fitness of bacterial cells. Such a evolution was clearly observed with the transition from the male- to the female-type, which indicated the independence of the sex determination from the temperature limit of the endpoint cells. The transition from the male- to the female-type was finally achieved. The transition from the male- to the female-type was finally achieved.

The authors identified a gene responsive to dopamine treatment, which showed higher expression in male embryos resulted in the occurrence of male-specific expression of soluble VEGFR1 (sVEGFR1). The model mice showed hyperresponsiveness and prothrombin during pregnancy, and the symptoms regressed after parturition. We further showed that pravastatin induced the VEGF-like factor from the placenta and ameliorated the symptoms. Our results strongly suggest that the interactions between the male-specific gene and the placenta provide insight into the molecular recognition of TNF by TNFR2. Comparison to the known TNFR1 structure highlighted several differences between the ligand binding interfaces of the two receptors.

This result may contribute to the design of therapeutic agents for autoimmune diseases.

The autocrine-immune disease development is believed to be a result of a breakdown in CD4+ T-cell tolerance for a tissue-specific-antigen. However, we show inactivation of CD4+ T cells by TCR-ligation in a TNF-dependent manner. Tumor necrosis factor (TNF) is an inflammatory cytokine that is important in the immune response, which are mediated through their receptors, TNFR1 and TNFR2. Antibody therapy based on TNF delivery against TNF administration can be used to treat several chronic autoimmune diseases; however, such treatment sometimes results in serious side effects, which are thought to be caused by the blocking of signals from both TNFRs. Therefore, knowledge of the structural basis for the recognition of TNF by each receptor would be invaluable in designing TNFR-selective drugs. Here, we solved the crystal structure of the TNF–TNFR2 complex, which provided insight into the molecular recognition of these tissues. This model provides a possible explanation for why tissue-specific-antigens recognized by activated CD4+ T-cells have not been identified in many MHCII autoimmune-diseases.

The greening ability of photosynthetic organisms is attributed to the role played by protochlorophyllide reductase (Pchlide) oxidoreductase in the formation of the direct precursor of chlorophyll (Chl). Two distinct types of enzymes catalyze the Pchlide reduction: light-dependent and dark-operative type enzymes. Dark-operative Pchlide oxidoreductase (DPOK) is a nitrogenase-like enzyme containing oxygen-sensing properties. In 2010, we identified the structural basis of the greening ability of plants in the dark through X-ray crystallographic analysis of the DPOK. The catalytic component of DPOK from the photosynthetic bacterium, Rhodobacter capsulatus, was crystallized in its Pchlide-bound and Pchlide-free forms, the structures were resolved to 2.3 and 2.8 Å resolution, respectively.