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### Links, Abstracts, Articles, etc.

These links should work as of 2014; sometimes you have to click on them several times; if they don't work, then Google/search the titles

Deiodinases, Extra-thyroidal T3 production, Iodine/NIS, Bromide, Amiodarone, Soy, SLC5, Mg/Se/Zn/Hg, Epitopes, Adenosine, Benzo's, BCAA's, Viruses, Mast Cells, IgG4-RD/EoE

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3673746/> The role of the iodothyronine deiodinases in the physiology and pathophysiology of thyroid hormone action. *"The source of most of the circulating T3 is D1-mediated, while D2 provides nuclear receptor-bound hormone. Using sensitive and specific assays, it has become apparent that both D2 and D3 are widespread throughout vertebrate tissues. The complex interactions between the activating D2 and the inactivating D3 in tissues expressing these two enzymes determine the intracellular T3 concentration. This provides enormous flexibility for both developmental and tissue regeneration processes, allowing exquisite control of intracellular T3 concentrations . . . However, since T4 is a prohormone, the systems controlling its secretion rate depend largely on the effects of the thyroid hormone receptor-bound T3 derived from it. Thus, the iodothyronine deiodinases which control the formation and degradation of T3 are critical to the maintenance of the euthyroid status".* (My note: DI's are both Selenoenzymes and peroxidases, both high on my target list for FQ's disruption mechanisms, either directly or via autoimmunity; note they are all integral membrane proteins as well; note suggestion of TKI's affecting D3; I question whether FQ's can act as TKI's, much as Sunitinib, a chemotherapeutic TKI)

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1578599/> Deiodinases: implications of the local control of thyroid hormone action

<http://joe.endocrinology-journals.org/content/190/2/363.long> Deiodinase type 1 activity is expressed in the prostate of pubescent rats and is modulated by thyroid hormones, prolactin and sex hormones.

## Extra-thyroidal T3 production

<http://ajpcell.physiology.org/content/294/5/C1227.long> H9c2 cardiomyoblasts produce thyroid hormone. "Thyroid hormone acts on a wide range of tissues. In the cardiovascular system, thyroid hormone is an important regulator of cardiac function and cardiovascular hemodynamics. Although some early reports in the literature suggested an unknown extrathyroidal source of thyroid hormone, it is currently thought to be produced exclusively in the thyroid gland, a highly specialized organ with the sole function of generating, storing, and secreting thyroid hormone. Whereas most of the proteins necessary for thyroid hormone synthesis are thought to be expressed exclusively in the thyroid gland, we now have found evidence that all of these proteins, i.e., thyroglobulin, DUOX1, DUOX2, the sodium-iodide symporter, pendrin, thyroid peroxidase, and thyroid-stimulating hormone receptor, are also expressed in cardiomyocytes."

[http://www.unboundmedicine.com/harriettlane/ub/citation/6266056/The\\_control\\_of\\_peroxidase\\_catalysed\\_iodination\\_and\\_de\\_iodination](http://www.unboundmedicine.com/harriettlane/ub/citation/6266056/The_control_of_peroxidase_catalysed_iodination_and_de_iodination) The control of peroxidase-catalysed iodination and de-iodination. "It has been demonstrated that the H<sub>2</sub>O<sub>2</sub>/I ratio is a critical factor in the control of iodination and de-iodination of covalently bound tyrosyl residues in proteins and free iodotyrosines by peroxidase enzymes. This has been shown for myeloperoxidase (MPO) isolated from normal human polymorphonuclear lymphocytes in particular, and also for peroxidase of animal origin such as thyroid peroxidase (TPO) and lactoperoxidase (LPO). It has been shown that the H<sub>2</sub>O<sub>2</sub>/I ratio exerts a controlling influence on MPO-catalysed reactions of fully iodinated tyrosines, e.g. di-iodotyrosine, and of partially and completely iodinated thyronines such as thyroxine and tri-iodothyronine. Using an in vivo model system it has been shown that MPO catalyses the sequential events of iodination, iodine exchange and de-iodination of tyrosines and, furthermore, that all three reactions are influenced by the rate of H<sub>2</sub>O<sub>2</sub> generation and the iodide concentration of the reaction medium. The action of MPO on iodothyronine substrates only affects de-iodination irrespective of whether the iodothyronine is partially iodinated, as in tri-iodothyronine, or completely iodinated, as in thyroxine. This MPO-catalysed de-iodination of thyroxine and tri-iodothyronine can also be regulated by the H<sub>2</sub>O<sub>2</sub>/I ratio. Moreover, the results show that MPO-catalysed iodine exchange can only occur in completely iodinated tyrosines such as di-iodotyrosine (DIT). Iodine exchange in partially iodinated tyrosines such as mono-iodotyrosine (MIT) or in iodothyronines (T3 and T4) cannot be catalysed by MPO irrespective of the H<sub>2</sub>O<sub>2</sub>/I ratio. These results introduce a new concept which may be important in understanding the control of thyroid activity in thyroid disease and the control of MPO activity in biological defence mechanisms in man." . . . "It is however known that the neutrophil, like the thyroid cell, possesses an active iodide concentration mechanism, can iodinate cell membranes of ingested bacteria and, in fact, is capable of extrathyroidal iodotyrosine and iodothyronine syntheses. In view of these common functional activities which are centered in their respective peroxidase enzymes, it is not surprising that some non-steroidal anti-inflammatory drugs as well as antithyroid substances will inhibit both MPO prepared from leucocytes and TPO obtained from thyroid cells."

<http://joe.endocrinology-journals.org/content/210/1/3.long> Extrathyroidal thyroid hormone synthesis?

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC185993/> Replacement Therapy for Hypothyroidism with Thyroxine Alone Does Not Ensure Euthyroidism in All Tissues, as Studied in Thyroidectomized Rats. "Intracellular T3 is derived from two sources: circulating T3, and local conversion of T4 to T3. The former is, moreover, not entirely derived from the thyroïdal secretion of T3, as a large proportion of circulating T3 has been generated from T4 in different tissues, and then released into the circulation. It was initially believed that circulating T3 would be in rapid and complete exchange with all of the T3 in extrathyroidal tissues, whether derived from the circulation or generated locally from T4. Therefore, under steady state conditions normal circulating T3 levels ought to ensure normal levels of T3 in all tissues. Studies from our laboratory (6, 7), however, questioned this assumption. Triiodothyronine generated locally from T4 is not necessarily in rapid or complete equilibrium with circulating T3 in all tissues, and therefore cannot be readily quantified from serum T3 levels and the tissue to plasma T3 ratio for that tissue, as determined with labeled T3. This was shown independently for anterior pituitary nuclear T3 by Silva and Larsen (8), and the important role of tissue deiodinative pathways for the regulation of intracellular sources of T3 was established (9). Different iodothyronine deiodinases were characterized and their different responses to thyroid status established" . . . "Despite the many gaps in our knowledge, it would appear likely that those tissues which derive most of their T3 from the circulation would have normal concentrations of T3 when circulating T3 levels are normal, whereas those tissues deriving all or most of their T3 by local generation from T4 would have normal T3 concentrations when plasma T4 is normal or somewhat elevated, provided the physiological responses to changes in thyroid status of the different deiodinases and of other regulatory mechanisms are not impaired."

<http://www.ncbi.nlm.nih.gov/pubmed/22791167> Influence of iodine-deficiency on thyroid hormones homeostasis in rats.

<http://www.ncbi.nlm.nih.gov/pubmed/7262025> Presence of L-thyroxine and 3,5,3'-triiodo-L-thyronine in tissues from thyroidectomized rats. "Female rats were killed 15 days, 2 months, and 4 months after surgical thyroidectomy that was followed by injection of 100 microCi <sup>131</sup>I. The concentrations of T3 and T4 were measured in tissues (liver, kidney, brain, heart, and hindleg muscle) specific RIAs. Results were compared to those found in intact rats. Thyroidectomy resulted in severe hypothyroidism by 2 and 4 months after the operation, as assessed by undetectable levels of T4 and T3 in unextracted plasma, high circulating TSH, hypothermia, stasis of body weight increase, and depletion of pituitary GH content. Concentrations of T4 and T3 in plasma, as determined after extraction and concentration, were very low, being less than 5% of the normal value by the earliest observation period (15 days). In contrast, although tissue concentrations and total organ contents also decreased after thyroidectomy, they were still clearly detectable 4 months after thyroidectomy. The rates of decrease of T4 and T3 concentrations in most tissues were markedly slower than expected from their rapid decrease in plasma. Some tissues still contained 20% of the normal level 2-4 months after ablation of the thyroid. Tissue levels of thyroid hormones were hardly detectable in rats thyroidectomized 6 months before, having decreased in most tissues to less than 5% of the normal value. Several animals from this group had died. It is concluded that tissues from severely hypothyroid thyroidectomized rats may contain higher concentrations of T4 and T3 than previously thought. The idea that thyroid hormone is not essential for life, based on the assumption

*that thyroidectomized animals survive without thyroid hormones, might have to be reevaluated.”* (My note: I strongly suspect that iodine stores can be utilized for localized (intracellular) T3/TH production in thyroidectomized animals as a “last ditch effort for survival following thyroidectomy without TH replacement”, but only for a limited time. I believe that TH is essential for life, and had the experiment gone on longer, more animals would have died. On the other hand, if animals continued to survive in this experiment beyond 6 months and much longer, then consideration to alternative pathways for TH productions should be sought – genomically as well [alternative gene pathways for iodine utilization or TH production “switched on” or epigenetic modifications])

<http://joe.endocrinology-journals.org/content/210/1/117.long> Influence of thyroidectomy on thyroxine metabolism and turnover rate in rats. “*Evans et al. (1960) reported that thyroidectomized (Tx) rats, whose growth had plateaued, could be made to grow again with a daily injection of large doses of inorganic iodide (3–5 mg/day). It has been subsequently shown that daily administration of 5 mg iodide to Tx rats partially restores their heart rate, metabolic rate, gonad and adrenal size and function, and pituitary acidophils (Evans et al. 1966). There are two potential mechanisms for this phenomenon: supply of thyroid hormones by extra-thyroidal tissues and repression of thyroid hormone degradation.*”

<http://www.ncbi.nlm.nih.gov/pubmed/683976> Effect of thyroid hormones and iodine ions on the amino acid incorporation into proteins of liver mitochondria. “*The results obtained confirmed the supposition that under definite conditions iodine ions could imitate the effect of the thyroid hormones on the protein synthesis in the cell of animals; the problem of a possibility of thyroid hormones to realize its biological effect at the molecular level with the aid of iodine ions is thus put forward.*”

<http://www.ncbi.nlm.nih.gov/pubmed/425369> Effect of triiodothyronine and ICl on protein synthesis in cell-free systems. “*The thyroid hormones and iodine ions stimulated protein synthesis in vitro in liver microsomes of thyroidectomized animals only after preincubation with mitochondria or nuclei . . . Thyroid hormones and iodine ions stimulated synthesis of specific factors in mitochondria (MBS) and in nuclei (NBS) of thyroidectomized rat liver tissue, which increased the protein synthesis in isolated microsomes in vitro.*”

<http://www.ncbi.nlm.nih.gov/pubmed/230474> Triiodothyronine binding by the liver nuclei and mitochondria. “*The binding of I125-triiodothyronine by male thyroidectomized rat liver nuclei and mitochondria in vivo and in vitro was studied. Labeled triiodothyronine was bound by the liver nuclei and mitochondria proteins. 90% radioactivity was bound by the nuclear nonhistone proteins. The binding of I125-triiodothyronine to the nuclei and mitochondria protein receptors was inhibited by unlabeled triiodothyronine and ICl. It is suggested that aromatic amino acids serve as the binding sites of the protein receptors, and that iodine atoms in the thyroid hormone molecules participated directly in the binding process.*”

<http://www.ncbi.nlm.nih.gov/pubmed/687810> Effect of in vivo thyroid hormones and IGL on protein synthesis in the mitochondria of thyroidectomized animals. “*T3 or IGL administration to thyroidectomized rats normalized protein synthesis in the liver mitochondria. According to all the biochemical indices studied the IGL effect was analogous to that of triiodothyronine. The absence of*

thyroid hormones in the organism of thyroidectomized animals, or T3 or IGL administration had no effect on the radioactivity of the free tyrosine pool in the liver tissue.”

<http://www.ncbi.nlm.nih.gov/pubmed/4450515> Thyroxine-like effect of iodine-containing compounds on the activity of pentosephosphate cycle enzymes.

<http://press.endocrine.org/doi/abs/10.1210/endo-78-5-983> Biological Evidence for Extrathyroidal Thyroxine Formation. *“The efficacy of iodide and thyroxine in ameliorating the several deficiencies occasioned by thyroidectomy in male and female rats was compared in order to obtain indirect evidence for extrathyroidal thyroxine formation. More direct refutation of the opposing concept that iodide simulates the action of thyroxine was also sought in experiments with propylthiouracil (PTU) and tribromothyronine. In all indices of thyroxine action examined in thyroidectomized rats, namely, growth, metabolic rate, heart rate, and pituitary, adrenal and reproductive function, the restorative or maintenance activities of large quantities of iodide were identical with those of minute quantities of thyroxine. Effective doses of iodide presumably resulted in the formation of thyroxine in quantities equivalent to the daily injection of 0.25–0.5 ng. PTU abolished most of the growth response to iodide, while not interfering with the action of thyroxine, which provided even more cogent evidence that the responses obtained were due to the formation of thyroxine. To further support the inference that the inhibitory influence of PTU was exercised through interference with iodothyronine formation rather than interference with the extrathyroidal intracellular oxidation of iodide to the potentially active substance iodine, it was necessary to analogize with the effects of tribromothyronine and bromide. Since tribromothyronine possessed high biological activity in thyroidectomized rats while bromide was inactive, it was concluded that the iodothyronine molecule functions in some manner other than that of a simple transmembrane transport system for oxidizable iodide. Although the results strongly suggest that extrathyroidal thyroxine formation does occur in the rat, these lines of evidence are still circumstantial. (Endocrinology 78: 983, 1966).”*

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3916908/> The biology of the sodium iodide symporter and its potential for targeted gene delivery.

<http://benthamscience.com/journal/abstracts.php?journalID=ccb&articleID=94619> Evolutionary Significance of Iodine. (Google title to access full PDF).

<http://www.jpands.org/vol11no4/millerd.pdf> Extrathyroidal Benefits of Iodine

## Iodine/NIS, Bromide, Amiodarone, SLC5, Soy

[http://www.scielo.br/scielo.php?script=sci\\_arttext&pid=S0004-27302007000500004&lng=en&nrm=iso&tlng=en](http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0004-27302007000500004&lng=en&nrm=iso&tlng=en) The Importance of Sodium/Iodide Symporter (NIS) for Thyroid Cancer Management

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3530113/> Dietary iodide controls its own absorption through post-transcriptional regulation of the intestinal Na<sup>+</sup>/I<sup>-</sup> symporter

<http://jeb.biologists.org/content/216/5/915.long> Iodine accumulation in sea urchin larvae is dependent on peroxide

[http://www.nutritionjrn.com/article/S0899-9007\(09\)00245-7/abstract](http://www.nutritionjrn.com/article/S0899-9007(09)00245-7/abstract) Iodine, Thymus, and Immunity. *“... extrathyroidal iodine has an important action on the immune system. The high iodide concentration of thymus provides the anatomic rationale for this role of iodine in the immune system.”* (My note: iodine, T3, and T4 caused mild to severe pain in my thymus gland (along with my thyroid gland) in Year 5 post (after a major iodine-induced flare), which supports this statement; in my case, I could not utilize iodine effectively post flox, which is why I assume I felt pain – also see references on hyperT causing thyc hypertrophy).

<http://jn.nutrition.org/content/127/6/1214.long> Dietary Iodine and Selenium Interact To Affect Thyroid Hormone Metabolism of Rats

<http://omicsonline.org/open-access/the-antitumor-activity-of-molecular-iodine-complexes-with-lithium-iaa.1000096.php?aid=25899> The Antitumor Activity of Molecular Iodine Complexes with Lithium Halogenides and Bioorganic Ligands when Applied in Combination with Doxorubicin

<http://www.ncbi.nlm.nih.gov/pubmed/10585592> Synergistic cytotoxicity of iodine-131-anti-CD20 monoclonal antibodies and chemotherapy for treatment of B-cell lymphomas.

<http://www.ncbi.nlm.nih.gov/pubmed/15169965> Iodine toxicity and its amelioration. *“Bromine can replace I on position 5 of both T(3) and T(4) with no loss of thyroid hormone activity. Avian work has also demonstrated that oral bromide salts can reverse the malaise and growth depressions caused by high doses of I (as KI) added as supplements to the diet.”*

<http://www.ncbi.nlm.nih.gov/pubmed/15119938> Metabolism of bromide and its interference with the metabolism of iodine.

<http://www.ncbi.nlm.nih.gov/pubmed/7710868> Effect of enhanced bromide intake on the concentration ratio I/Br in the rat thyroid gland.

<http://www.ncbi.nlm.nih.gov/pubmed/12065227> Impact of high bromide intake in the rat dam on iodine transfer to the sucklings.

<http://www.ncbi.nlm.nih.gov/pubmed/11697761> Effect of high bromide levels in the organism on the biological half-life of iodine in the rat.

<http://www.ncbi.nlm.nih.gov/pubmed/9728485> Biological half-life of bromine in the rat thyroid.

<http://www.ncbi.nlm.nih.gov/pubmed/9542578> Long-term action of potassium bromide on the rat thyroid gland.

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3063534/> Iodine, Iodine Metabolism and Iodine Deficiency Disorders Revisited.

<http://www.ncbi.nlm.nih.gov/pubmed/21690268> Antineoplastic effect of iodine and iodide in dimethylbenz[a]anthracene-induced mammary tumors: association between lactoperoxidase and estrogen-adduct production Note: iodine alone is anti-neoplastic. Note: "LPO, a protein homolog of TPO, oxidizes iodide and binds it to the lactoprotein casein, which is secreted together with free iodide into the milk" Note: consider dairy "allergies" or sensitivities LPO related for TPO positive patients?

<http://joe.endocrinology-journals.org/content/208/1/89.long> Inhibition of intrathyroidal dehalogenation by iodide

<http://icb.oxfordjournals.org/content/49/2/155.long> Evolutionary roots of iodine and thyroid hormones in cell–cell signaling. *"It is now widely accepted that photosynthetic alpha-proteobacteria became the mitochondria of eukaryotic cells . . . Since it is clear that such organisms probably possessed iodotyrosines (the precursors of THs), it should come as no surprise that the primary sites of action for THs, at least in vertebrates, are in mitochondria . . . In vertebrates, THs up-regulate the production of the ATPase enzyme that drives this potassium-sodium pump . . . In vertebrates, THs also up-regulate mtDNA replication, enabling cells to increase the absolute number of mitochondria available to generate energy when needed. THs also up-regulate the expression of many mitochondrial genes in muscle cells at work . . . Iodinated tyrosines probably became important about this time, in part, because they were good catalysts, reacted readily with others to form new complex molecules, and moved easily through permeable membranes. It is probable that iodinated tyrosines became regulators of ATPase production in early mitochondria and if so, their role as gene regulators may predate the first eukaryotes (this hypothesis can be tested experimentally by investigating whether iodinated tyrosines or their derivatives are able to up-regulate the production of ATPase in non-vertebrate mitochondria). Due to the fact that iodinated tyrosines could move easily between cells, they were likely utilized as cell–cell signaling molecules in multicellular organisms, especially for the coordinated operation of mitochondrial metabolism (including regulation of essential genes) as well as for replication of mtDNA."*

<http://www.atsdr.cdc.gov/toxprofiles/tp158.pdf> Draft Toxicological Profile For Iodine

<http://jnm.snmjournals.org/content/14/6/331.full.pdf> 99mTCPERTECH N ETATE TRANSPORT IN MAN: ABSORPTION AFTER SUBCUTANEOUS AND ORAL ADMINISTRATION; SECRETION INTO SALIVA AND GASTRIC JUICE

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4089555/> Iodide transport: implications for health and disease. ". . . *The most important dietary sources of iodine in industrialized countries are breads containing iodized salt and milk. Iodide absorption in the gastrointestinal tract is mediated by the sodium-iodide symporter (NIS).*" (My note: Good paper overall).

<http://ejournal-online.org/content/140/3/241.long> Amiodarone compared with iodine exhibits a potent and persistent inhibitory effect on TSH-stimulated cAMP production in vitro: a possible mechanism to explain amiodarone-induced hypothyroidism.

<http://ejournal-online.org/content/137/1/89.long> Amiodarone induces a different pattern of ultrastructural change in the thyroid to iodine excess alone in both the BB/W rat and the Wistar rat.

<http://emedicine.medscape.com/article/129033-overview> Thyroid Dysfunction Induced by Amiodarone Therapy

[http://www.academia.edu/2007862/EVOLUTION\\_OF\\_DIETARY\\_ANTIOXIDANTS](http://www.academia.edu/2007862/EVOLUTION_OF_DIETARY_ANTIOXIDANTS) EVOLUTION of DIETARY ANTIOXIDANTS DEFENCES (author = Venturi).

<http://www.ncbi.nlm.nih.gov/pubmed/12390328> The sodium iodide symporter: its pathophysiological and therapeutic implications.

<http://www.ncbi.nlm.nih.gov/pubmed/12488351> Anion selectivity by the sodium iodide symporter.

[http://optimox.com/pics/Iodine/IOD-13/IOD\\_13.htm](http://optimox.com/pics/Iodine/IOD-13/IOD_13.htm) The Saliva/Serum Iodide Ratio as an Index of Sodium Iodide Symporter Efficiency

<http://www.ibiomedsci.com/content/17/1/89> Conserved charged amino acid residues in the extracellular region of sodium/iodide symporter are critical for iodide transport activity. *“NIS is a member of solute-sodium symporters. Solute-sodium symporters are a large family of proteins that co-transport sodium ions with sugars, amino acids, vitamins, or iodide . . . . In this study, we elucidated the importance of 14 conserved charged amino acid residues, which were located in the extracellular region of NIS, by site-directed mutagenesis and kinetic analysis. Our findings indicated that all mutants, except R9A, displayed severe defects on the iodide uptake. Moreover, mutations at positively charged amino acid residues led to the decrease in Vmax, while mutations at negatively charged residues resulted in the increase in Km. Our data suggested that conserved charged amino acid residues, except Arg-9, in the extracellular region of NIS were critical for iodide transport.”*

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3367315/> The Sodium Iodide Symporter (NIS) as an Imaging Reporter for Gene, Viral, and Cell-based Therapies

<http://www.ncbi.nlm.nih.gov/pubmed/11396700> Sodium Iodide Symporter in Health and Disease

<http://www.ncbi.nlm.nih.gov/pubmed/12588808> The Sodium/Iodide Symporter (NIS): Characterization, Regulation, and Medical Significance

<http://ejournal-online.org/content/138/4/374.long> The sodium iodide symporter: its emerging relevance to clinical thyroidology

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3012967/> Surprising Substrate Versatility in SLC5A6: Na<sup>+</sup>-COUPLED I<sup>-</sup> TRANSPORT BY THE HUMAN Na<sup>+</sup>/MULTIVITAMIN TRANSPORTER (hSMVT).

*“Because hSMVT is found in the intestine and in many other tissues, we propose that hSMVT may play*

*an important role in the homeostasis of I<sup>-</sup> in the body. . . . In addition, the other substrates of hSMVT, namely, PA [pantothenic acid], biotin, and LA [alpha lipoic acid], specifically inhibit I<sup>-</sup> transport, suggesting a common uptake mechanism that is shared among these structurally diverse substrates. As hSMVT is universally expressed in all tissues of the human body, it is feasible to speculate that hSMVT contributes to the homeostasis of I<sup>-</sup> in the body. . . . Taken together, our results unequivocally show that hSMVT, in addition to transporting biotin and pantothenic acid, catalyzes Na<sup>+</sup>/I<sup>-</sup> and Na<sup>+</sup>/alpha-lipoic acid co-transport(symport) with the electrochemical Na gradient as the immediate driving force.”*

<http://www.ncbi.nlm.nih.gov/pubmed/10566669> Analysis of human sodium iodide symporter immunoreactivity in human exocrine glands.

<http://physiologyonline.physiology.org/content/19/6/370> Surprising versatility of Na<sup>+</sup>-glucose cotransporters: SLC5.

<http://www.ncbi.nlm.nih.gov/pubmed/4029592> Thyroid Morphological and Functional Heterogeneity: Impact on Iodine Secretion

<http://carcin.oxfordjournals.org/content/21/4/707.long> Dramatic synergism between excess soybean intake and iodine deficiency on the development of rat thyroid hyperplasia.

<http://www.ncbi.nlm.nih.gov/pubmed/19569179> Endogenous expression of the sodium iodide symporter mediates uptake of iodide in murine models of colorectal carcinoma

<http://www.ncbi.nlm.nih.gov/pubmed/12354616> The sodium/substrate symporter family: structural and functional features

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3496787/> Structure and function of Na<sup>+</sup>-symporters with inverted repeats

<http://www.ncbi.nlm.nih.gov/pubmed/9589686> Analysis of human sodium iodide symporter gene expression in extrathyroidal tissues and cloning of its complementary deoxyribonucleic acids from salivary gland, mammary gland, and gastric mucosa.

<http://www.ncbi.nlm.nih.gov/pubmed/23918874> Soy extracts suppressed iodine uptake and stimulated the production of autoimmunogen in rat thyrocytes. *“Soy consumption is associated with thyroid disorders such as hypothyroidism, goiter, and autoimmune thyroid disease (ATD) as well as increased iodine requirement in certain cases. . . . soy remarkably inhibited iodide uptake in the FRTL cells. Soy ISF, particularly genistein, induced the production of P40, which might be responsible for the higher incidence of ATD reported in soy infant formula-fed children.”*

<http://www.ncbi.nlm.nih.gov/pubmed/23155081> Iodine accumulation in sea urchin larvae is dependent on peroxide

<http://www.ncbi.nlm.nih.gov/pubmed/12448768> Influence of lithium on growth and viability of thyroid follicular cells. *“Lithium accumulates in the thyroid gland and can cause goiter or thyroid dysfunction.”*

# Mg/Se/Zn/Hg

<http://www.ncbi.nlm.nih.gov/pubmed/8930527> Magnesium Metabolism in Hyperthyroidism. *"The influence of thyroid hormones on magnesium homeostasis is well known, but not enough attention is paid to magnesium metabolism in hyperthyroidism. These observations clearly indicate that in Graves' disease, the magnitude of magnesium metabolism alteration is closely related to the extent of the increase in thyroid hormones in plasma."*

<http://www.jbc.org/content/226/2/597.full.pdf> THE EFFECT OF THYROXINE ON MAGNESIUM REQUIREMENT *"Furthermore, the concentration of serum magnesium is lower in thyrotoxic patients and, upon treatment, serum magnesium levels return to near normal.' Such patients may require higher intakes of magnesium than normal to attain magnesium balance."*

<http://jn.nutrition.org/content/77/4/455.full.pdf> Magnesium and Thyroid Function in the Rat

<http://www.bmj.com/rapid-response/2011/10/27/magnesium-thyroxine-and-uncoupling-proteins> Magnesium, Thyroxine and Uncoupling Proteins *"Magnesium is principally an intracellular cation and, as with most minerals and vitamins, plays an essential role in many metabolic processes including those hormonally and enzymatically driven. Magnesium deficiency, in its slightest form and before the appearance of any clinical signs in the experimental animal, uncouples oxidative phosphorylation in isolated mitochondrial preparations and the effect is compounded by thyroxine administration or in hyperthyroidism. One other interesting facet, somewhat related to "energy conservation/expenditure" metabolism, is that during hibernation, hypermagnesemia occurs in hibernating animals conserving energy with a marked bradycardia. It would be reasonable to assume that whatever these "uncoupling" proteins are, that magnesium, and perhaps other electrolytes, are interacting in energy saving/wasting biological reactions. The literature on the inter-relations between magnesium metabolism and thyroid status goes back to the 1930's."*

<http://www.soilandhealth.org/01aglibrary/010106voisin/010106gtchap22.html> Grass Tetany: Thyroid, lactation, temperature and magnesium requirements

<http://www.iasj.net/iasj?func=fulltext&ald=43622> Chemical Study of Antithyroid Peroxidase Auto Antibodies, Magnesium and Cobalt in Hyperthyroidism Patients From Different Regions of Iraq. *"Mg and Co were altered in response to thyroid hormones . . .the present study is in agreement with other reports which found which found lower serum levels of magnesium in hyperthyroidism patients. Some data suggest that thyroid hormone has a direct effect on the tubule which favors the retention of Mg"*.

<http://jasn.asnjournals.org/content/20/11/2291.long> Clinical Consequences and Management of Hypomagnesemia

<http://www.ncbi.nlm.nih.gov/pubmed/2810922> Plasma and Erythrocyte Magnesium Concentrations in Thyroid Disease: Relation to Thyroid Function and the Duration of Illness . *"These results suggest that magnesium metabolism in thyroid dysfunction is affected not only by thyroid hormone levels but also by the duration of illness"*.

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC292768/> Magnesium Metabolism in Hyperthyroidism and Hypothyroidism

[https://www.jstage.jst.go.jp/article/tjem1920/96/1/96\\_1\\_1/article](https://www.jstage.jst.go.jp/article/tjem1920/96/1/96_1_1/article) Magnesium Metabolism in Thyroid Dysfunction

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC435075/> MAGNESIUM PARTITION STUDIES IN GRAVES' DISEASE AND IN CLINICAL AND EXPERIMENTAL HYPOTHYROIDISM

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1236005/> Effects of Thyroid Status on Renal Calcium and Magnesium Handling

<http://www.fasebj.org/content/25/1/370.long> Effects of selenite and chelating agents on mammalian thioredoxin reductase inhibited by mercury: implications for treatment of mercury poisoning

<http://www.jbc.org/content/283/18/11913.long> Inhibition of the Human Thioredoxin System A MOLECULAR MECHANISM OF MERCURY TOXICITY

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1280813/> Voltage-dependent block by intracellular Mg<sup>2+</sup> of N-methyl-D-aspartate-activated channels

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2912286/> Regulation and function of selenoproteins in human disease. *“Selenium deficiency and mutations or polymorphisms in selenoprotein genes and synthesis cofactors are implicated in a variety of diseases, including muscle and cardiovascular disorders, immune dysfunction, cancer, neurological disorders and endocrine function. Members of this unusual family of proteins have roles in a variety of cell processes and diseases.”*

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2866081/> The human selenoproteome: recent insights into functions and regulation

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3937696/> Interplay between Selenium Levels, Selenoprotein Expression and Replicative Senescence in WI-38 Human Fibroblasts

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3723386/> The influence of selenium on immune responses

<http://www.researchgate.net/publication/36362097> [The effect of estrogen status on selenium metabolism in female rats electronic resource](#) THE EFFECT OF ESTROGEN STATUS ON SELENIUM METABOLISM IN FEMALE RATS

<http://www.ncbi.nlm.nih.gov/pubmed/19332511> Statin-Induced Liver Injury Involves Cross-Talk between Cholesterol and Selenoprotein Biosynthetic Pathways. *“Here, we report our finding that atorvastatin, cerivastatin, and lovastatin at clinically common concentrations induce a selective, differential loss of selenoprotein expression in cultured human HepG2 hepatocytes. The primarily affected selenoprotein was glutathione peroxidase (GPx), whose biosynthesis, steady-state expression level, and catalytic activity were significantly reduced with 10 to 100 nM concentrations of the different*

compounds. Messenger RNA levels of GPx1 and GPx4 were unaffected by statin treatment, pointing at a post-transcriptional mechanism of selenoprotein suppression”.

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2424839/> Zinc metabolism in thyroid disease.

*“Increased urinary zinc concentrations may result from increased tissue catabolism such as muscle. The results of this study suggest that abnormal zinc metabolism occurs commonly in patients with thyroid disease.”*

## Epitopes

<http://www.tandfonline.com/doi/pdf/10.1080/02648725.2007.10648092> Mapping the Epitopes of Antibodies

<http://www.biomedcentral.com/1472-6807/7/64> Antibody-protein interactions: benchmark datasets and prediction tools evaluation

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1782462/> Thyroglobulin as an autoantigen: what can we learn about immunopathogenicity from the correlation of antigenic properties with protein structure? *“Autoantibodies against human thyroglobulin are a hallmark of autoimmune thyroid disease in humans, and are often found in normal subjects. Their pathogenic significance is debated . . . A number of T-cell epitope-bearing peptides, endowed with thyroiditogenic power in susceptible mice, were also identified . . . More than half of them are located within the acetylcholinesterase-homologous domain of thyroglobulin, and overlap B-cell epitopes associated with autoimmune thyroid disease . . .”*

<http://www.jbc.org/content/279/37/39058.full> Directed Mutagenesis in Region 713-720 of Human Thyroperoxidase Assigns 713KFPED717 Residues as Being Involved in the B Domain of the Discontinuous Immunodominant Region Recognized by Human Autoantibodies. *“Autoantibodies (aAbs) to thyroid peroxidase (TPO), the hallmark of autoimmune thyroid disease (AITD), recognize conformational epitopes restricted to an immunodominant region (IDR), divided into two overlapping domains A and B. Despite numerous efforts aimed at localizing the IDR and identifying aAb-interacting residues on TPO, only two critical amino acids, Lys713 and Tyr772, have been characterized . . . this study definitively identifies the amino acids Lys713-Asp717 as being the key residues recognized by IDR/B-specific anti-TPO aAbs in AITD.”*

<http://www.ncbi.nlm.nih.gov/pubmed/11129117> Autoimmune response to the thyroid in humans: thyroid peroxidase--the common autoantigenic denominator. *“Autoimmunity to thyroid peroxidase (TPO), manifest as high affinity IgG class autoantibodies, is the common denominator of human thyroid autoimmunity, encompassing patients with overt hyper- or hypothyroidism as well as euthyroid individuals with subclinical disease.”*

<http://www.ncbi.nlm.nih.gov/pubmed/17822378> Thyroid peroxidase as an autoantigen. *“Amino acids recognized by TPOAbs are located in the regions with homology to myeloperoxidase (MPO) and the*

complement **control protein (CCP)** but not in the epidermal growth factor (EGF)-like region. **T cells** recognize epitopes in the **MPO-like region** but not in the CCP- or EGF-like regions in humans.”

<http://www.ncbi.nlm.nih.gov/pubmed/16735377> The key residues in the immunodominant region 353–363 of human thyroid peroxidase were identified

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC298901/> Human thyroid peroxidase: Complete cDNA and protein sequence, chromosome mapping, and identification of two alternately spliced mRNAs

## Adenosine

<http://www.ncbi.nlm.nih.gov/pubmed/6313325> Evidence that organic iodine attenuates the adenosine 3',5'-monophosphate response to thyrotropin stimulation in thyroid tissue by an action at or near the adenylate cyclase catalytic unit

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3930074/> Adenosine receptors as drug targets — what are the challenges? “ . . . methylxanthines such as caffeine have profound biological effects as antagonists at adenosine receptors . . . There is strong evidence that adenosine has a functional role in many diseases . . . It is well known that adenosine is an important intermediary metabolite, acting as a building block for nucleic acids and a component of the biological energy currency ATP. In addition, adenosine functions as a signaling molecule through the activation of four distinct adenosine receptors — denoted A1, A2A, A2B and A3. These receptors are widely expressed and have been implicated in several biological functions, both physiological and pathological. These include cardiac rhythm and circulation, lipolysis, renal blood flow, immune function, sleep regulation and angiogenesis, as well as inflammatory diseases, ischaemia-reperfusion and neurodegenerative disorders . . . The greatest challenge in developing adenosine receptor ligands for specific clinical applications is that adenosine signaling is so widespread. Adenosine itself is present ubiquitously, adenosine receptors are widely distributed throughout the body and adenosine acting at these receptors exerts a broad spectrum of physiological and pathophysiological functions.”

<http://www.hindawi.com/journals/jtr/2013/434727/> New Approaches to Thyroid Hormones and Purinergic Signaling. “It is known that thyroid hormones influence a wide variety of events at the molecular, cellular, and functional levels. Thyroid hormones (TH) play pivotal roles in growth, cell proliferation, differentiation, apoptosis, development, and metabolic homeostasis via thyroid hormone receptors (TRs) by controlling the expression of TR target genes. Most of these effects result in pathological and physiological events and are already well described in the literature. Even so, many recent studies have been devoted to bringing new information on problems in controlling the synthesis and release of these hormones and to elucidating mechanisms of the action of these hormones unconventionally. The purinergic system was recently linked to thyroid diseases, including enzymes, receptors, and enzyme products related to neurotransmitter release, nociception, behavior, and other

vascular systems. Thus, throughout this text we intend to relate the relationship between the TH in physiological and pathological situations with the purinergic signaling.”

<http://www.iasj.net/iasj?func=fulltext&ald=35617> A Study on the Relationship between Thyroid Hormones and Adenosine Deaminase Enzyme Activity in Patients with Auto- Immune Hyperthyroid Disease

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1148310/> Thyroid status and adenosine content of adipose tissue. *“Thyroid hormones play a permissive role in peripheral tissues, rendering them sensitive to the effects of catecholamines.”*

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1572083/> Thyrotropin regulates adenosine A1 receptor expression in rat thyroid FRTL-5 cells

<http://www.ncbi.nlm.nih.gov/pubmed/2832439> Pathogenesis of autonomous thyroid nodules: in vitro study of iodine and adenosine 3',5'-monophosphate metabolism.

<http://www.sciencedirect.com/science/article/pii/0304416572902929> Regulation of iodine metabolism in human leukocytes by adenosine 3',5'-monophosphate. *“The rate of iodide uptake and formation of iodo-compounds in human leukocytes is regulated by adenosine 3',5'-monophosphate (cyclic AMP).”*

[http://www.researchgate.net/publication/7250325\\_Amidarone\\_inhibits\\_thyroidal\\_iodide\\_transport\\_in\\_vitro\\_by\\_a\\_cyclic\\_adenosine\\_5'-monophosphate-\\_and\\_iodine-independent\\_mechanism](http://www.researchgate.net/publication/7250325_Amidarone_inhibits_thyroidal_iodide_transport_in_vitro_by_a_cyclic_adenosine_5'-monophosphate-_and_iodine-independent_mechanism) Amiodarone inhibits thyroidal iodide transport in vitro by a cyclic adenosine 5'-monophosphate- and iodine-independent mechanism. *“The iodine-free AM analog dronedarone also inhibited 125I- transport to the same extent as AM. The findings indicate that AM blocks thyroidal iodide uptake by reducing the iodide permeability of the apical plasma membrane of the thyroid epithelial cells. The effect is iodine independent and long-lasting and does not involve impaired function of NIS or the TSH receptor/cAMP signaling pathway”.* (My note: note that dronedarone also inhibited – more evidence that it is not iodine itself that is “toxic”).

## Benzo's

<http://www.ncbi.nlm.nih.gov/pubmed/15500492> Paradoxical reaction following intravenous midazolam premedication in pediatric patients – a randomized placebo controlled trial of ketamine for rapid tranquilization.

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2047018/> Self-harm and suicide associated with benzodiazepine usage

## BCAA's

<http://www.ncbi.nlm.nih.gov/pubmed/24651065> Branched-chain amino acid metabolism: from rare Mendelian diseases to more common disorders.

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3695706/> Interplay between Lipids and Branched-Chain Amino Acids in Development of Insulin Resistance

<http://jac.oxfordjournals.org/content/58/6/1264.full.pdf> High-level resistance to moxifloxacin and gatifloxacin associated with a novel mutation in gyrB in toxin-A-negative, toxin-B-positive *Clostridium difficile*

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1346767/> Global Transcriptome Analysis of the Responses of a Fluoroquinolone-Resistant *Streptococcus pneumoniae* Mutant and Its Parent to Ciprofloxacin

<http://www.biomedcentral.com/content/pdf/1471-2180-13-50.pdf> Comparative transcription analysis and toxin production of two fluoroquinolone-resistant mutants of *Clostridium perfringens*

<http://www.hchs.edu/literature/BCAA.pdf> A Primer On Branched Chain Amino Acids

<http://jn.nutrition.org/content/135/6/1557S.short> Branched-Chain Amino Acid Metabolism: Implications for Establishing Safe Intakes

**Viruses** (Looking for commonalities in mechanisms of action (direct/autoimmune) between viruses and FQ's (and consider Lyme's too) – glutamine/glutamic acid, ACH-related, HERV's?)

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC31166/> Cytomegalovirus in autoimmunity: T cell crossreactivity to viral antigen and autoantigen glutamic acid decarboxylase

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC329775/> Molecular Mimicry and Myasthenia Gravis

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2589619/> The Acetylcholine Receptor as a Cellular Receptor for Rabies Virus *"In addition to clarifying aspects of rabies virus pathogenesis, these studies have broad implications regarding the mechanism by which other viruses or viral immunizations might mediate autoimmune diseases such as myasthenia gravis."*

<http://vir.sgmjournals.org/content/77/10/2437.long> Rabies virus binding to the nicotinic acetylcholine receptor alpha subunit demonstrated by virus overlay protein binding assay

<http://jvi.asm.org/content/72/9/7181.abstract> The Neural Cell Adhesion Molecule Is a Receptor for Rabies Virus

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3993723/> Vaccinia Virus Requires Glutamine but Not Glucose for Efficient Replication “*Glutamine and glucose represent the two main carbon sources for mammalian cells . . . Viruses are dependent on the metabolic machinery of the host cell to supply the energy and molecular building blocks needed for critical processes including genome replication, viral protein synthesis, and membrane production. This study investigates how vaccinia virus (VACV) infection alters global cellular metabolism, providing the first metabolomic analysis for a member of the poxvirus family. Unlike most viruses examined to date, VACV does not activate glycolysis, and exogenous glucose is not required for maximal virus production. Instead, VACV requires exogenous glutamine for efficient replication, and inhibition of glutamine metabolism effectively blocks VACV protein synthesis. This study defines a major metabolic perturbation essential for the replication of a poxvirus and may lead to the discovery of novel antiviral therapies based on metabolic inhibitors.*”

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC355338/> Effects of L-Glutamine Deprivation on Growth of HVJ (Sendai Virus) in BHK Cells

<http://jvi.asm.org/content/84/4/1867> Glutamine Metabolism Is Essential for Human Cytomegalovirus Infection. “*This suggested that during infection, glutamine is used to fill the tricarboxylic acid (TCA) cycle (anaplerosis). In agreement with this, levels of glutamine uptake and ammonia production increased in infected cells, as did the activities of glutaminase and glutamate dehydrogenase, the enzymes needed to convert glutamine to alpha-ketoglutarate to enter the TCA cycle*”.

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3130066/> Viral effects on metabolism: changes in glucose and glutamine utilization during human cytomegalovirus infection. “*Human cytomegalovirus (HCMV) infection causes dramatic alterations of intermediary metabolism, similar to those found in tumor cells*”.

<http://vir.sgmjournals.org/content/67/10/2207.long> Glutamine Starvation of Murine Leukaemia Virus-infected Cells Inhibits the Read through of the gag-pol Genes and Proteolytic Processing of the gag Polyprotein

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC110918/> Borna Disease Virus Persistence Causes Inhibition of Glutamate Uptake by Feline Primary Cortical Astrocytes

<http://www.jneurosci.org/content/24/34/7566.long> Viral-Induced Spinal Motor Neuron Death Is Non-Cell-Autonomous and Involves Glutamate Excitotoxicity. “*These studies suggest that NSV infection triggers a cascade of events in the spinal cord resulting in impaired astrocytic glutamate transport and excitotoxic injury of motor neurons mediated via calcium-permeable AMPA receptors. Similar changes may occur in other motor neuron disorders such as amyotrophic lateral sclerosis or West Nile Virus-induced poliomyelitis, suggesting a common tissue injury pathway*”.

<http://www.newscientist.com/article/mg22630183.800#VTiK5WdMty0> Virus hiding in our genome protects early human embryos

<http://www.newscientist.com/article/mg20527451.200-i-virus-why-youre-only-half-human.html>

[http://en.wikipedia.org/wiki/Endogenous\\_retrovirus](http://en.wikipedia.org/wiki/Endogenous_retrovirus)

[http://en.wikipedia.org/wiki/Endogenous\\_viral\\_element](http://en.wikipedia.org/wiki/Endogenous_viral_element)

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1187282/> Demystified . . . Human endogenous retroviruses

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1009896/> Retroviruses in rheumatic diseases

<http://www.ncbi.nlm.nih.gov/pubmed/10454005> Molecular investigations implicate human endogenous retroviruses as mediators of anti-retroviral antibodies in autoimmune rheumatic disease.

## Mast Cells

<http://www.jimmunol.org/content/179/5/2673.full> **The Multitasking Mast Cell: Positive and Negative Roles in the Progression of Autoimmunity.** *“Among the potential outcomes of an aberrantly functioning immune system are allergic disease and autoimmunity. Although it has been assumed that the underlying mechanisms mediating these conditions are completely different, recent evidence shows that mast cells provide a common link. Mast cells reside in most tissues, are particularly prevalent at sites of Ag entry, and act as sentinel cells of the immune system. They express many inflammatory mediators that affect both innate and adaptive cellular function. They contribute to pathologic allergic inflammation but also serve an important protective role in bacterial and parasite infections. Given the proinflammatory nature of autoimmune responses, it is not surprising that studies using murine models of autoimmunity clearly implicate mast cells in the initiation and/or progression of autoimmune disease. In this review, we discuss the defined and hypothesized mechanisms of mast cell influence on autoimmune diseases, including their surprising and newly discovered role as anti-inflammatory cells.”*

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1298791/pdf/taos00014-0583.pdf> CHARACTERIZATION OF THE CHOROICAL MAST CELL

<http://www.ncbi.nlm.nih.gov/pubmed/23450078> A case of levofloxacin-induced anaphylaxis with elevated serum tryptase levels.

<http://www.ncbi.nlm.nih.gov/pubmed/19203807> Kounis syndrome: two extraordinary cases. Cardiac death due to Cipro

<http://www.ncbi.nlm.nih.gov/pubmed/11482521> Differential response of mast cells separated from various organs and basophils of dogs to the fluoroquinolone antimicrobial levofloxacin. “. . . indicating that LVFX preferably activated the **connective tissue-type mast cells** rather than the mucosal-type mast cells”.

<http://www.ncbi.nlm.nih.gov/pubmed/8597878> Flush induced by fluoroquinolones in canine skin.

<http://www.ncbi.nlm.nih.gov/pubmed/7852031> Effect of levofloxacin and ciprofloxacin injection on permeability of the tail vein in mice and skin microvasculature in rats.

<http://www.ncbi.nlm.nih.gov/pubmed/17502945> Increased mast cell density and microvessel density in the thymus of patients with myasthenia gravis.

<http://www.ncbi.nlm.nih.gov/pubmed/4055079> Thymus dependence of connective tissue mast cells: a quantitative cytofluorometric study of the growth of peritoneal mast cells in normal and athymic rats.

<http://www.ncbi.nlm.nih.gov/pubmed/809349> Mast cell sensitizing antibodies in myasthenia gravis. “Mast Cells Sensitizing Antibodies (MCSAb) were detected in patients with Myasthenia Gravis (MGr), by the Indirect Mast Cell Degranulation (IMCD). In most of the examined sera a correlation could be established between MCSAb and fluorescent antibodies to **muscle and to thymus**. The MCSAb were **specific for muscle extract**. They were resistant to prolonged heating and their reactivity in the IMCD test was not complement depending. Presence of MCSAb in sera of patients with MGr evidences the auto-allergic features of this disease”.

<http://www.researchgate.net/publication/6629536> [Nerve growth factor immunoreactivity of mast cells in acute involuted human thymus](#) Nerve growth factor immunoreactivity of mast cells in acute involuted human thymus.

<http://arthritis-research.com/content/pdf/ar4374.pdf> Mast cells exert pro-inflammatory effects of relevance to the pathophysiology of tendinopathy

<http://www.ncbi.nlm.nih.gov/pubmed/25316126> Relationship between serotonin and mast cells: inhibitory effect of anti-serotonin.

<http://www.ncbi.nlm.nih.gov/pubmed/6411454> **Influence of mast cells on thyroid function. “. . . confirmed the active participation of mast cells on TRH and/or TSH secretion.”**

<http://alwaywellwithin.com/resources/wellness/mast-cell-activation/> **Mast Cell Activation. Good site about this disorder, people with multiple chemical sensitivities, perhaps some FQ victims have this?**

<http://www.ncbi.nlm.nih.gov/pubmed/19456362> **Thyroid status can influence brain mast cell population.** “Treatment with tizoxin (T4) does not modify number or activational state of brain mast cells, whereas administration of the **antithyroid agent 6-n-propyl-2-thiouracil induces a significant increase (up to 40%) in the mast cell number within the telencephalon and diencephalon.** Hypophysectomy induces a significant decrease (up to 65%) of mast cells in all brain regions, whereas

*the pituitary homogenate augments their number. The results suggest that the pituitary-thyroid axis may be involved in the regulation of brain mast cell population.*"

<http://www.ncbi.nlm.nih.gov/pubmed/2462344> The interdependence of the follicular, parafollicular, and mast cells in the mammalian thyroid gland: a review and a synthesis.

<http://press.endocrine.org/doi/abs/10.1210/endo-92-1-152> Species Differences in Mast Cells of the Thyroid Gland. *"Mast cells in the thyroid gland of different mammalian species were compared with respect to endogenous 5-hydroxytryptamine (5-HT) content, ability to store 5-HT synthesized from its administered exogenous precursor, 5-hydroxytryptophan (5-HTP), ability to take up and store exogenous 5-HT, and the ultrastructure of the specific granules."*

<http://press.endocrine.org/doi/abs/10.1210/endo-90-3-802> Significance of Thyroid Mast Cells in Thyroid Hormone Secretion

<http://www.ncbi.nlm.nih.gov/pubmed/11792009> Estrogen regulates cytokine release in human mast cells.

<http://www.cricyt.edu.ar/biocell/vol/pdf/26/02.pdf> Estrogen receptors in mast cells from arterial walls

<http://link.springer.com/article/10.1007/BF00804248> Role of the mast cells in peroxidase activity of the thyroid gland in experimental burns

[http://www.researchgate.net/publication/257908315\\_Atrazine-induced\\_degranulation\\_of\\_thyroid\\_mast\\_cells\\_in\\_peripubertal\\_and\\_adult\\_rats](http://www.researchgate.net/publication/257908315_Atrazine-induced_degranulation_of_thyroid_mast_cells_in_peripubertal_and_adult_rats) Atrazine-induced degranulation of thyroid mast cells in peripubertal and adult rats

<http://www.ncbi.nlm.nih.gov/pubmed/10884184> Growth factor-expressing mast cells accumulate at the thyroid tissue-regenerative site of subacute thyroiditis. *"The data suggest that growth factor-expressing mast cells may play crucial roles in the thyroid tissue repair of subacute thyroiditis, modulating thyroid folliculogenesis and angiogenesis; and that the multifunctionality of the cells may be partly dependent on their expressions of various growth factors."*

<http://www.ncbi.nlm.nih.gov/pubmed/12500262> Mast cells and angiogenesis. *"There is much evidence that angiogenesis is related to mast cells . . . Mast cell products such as tryptase also degrade connective tissue matrix to provide space for neovascular sprouts."*

<http://onlinelibrary.wiley.com/doi/10.1111/j.1742-4658.2006.05211.x/full> Biology of mast cell tryptase

<http://www.ncbi.nlm.nih.gov/pubmed/15170507> Mast cell tryptase, a still enigmatic enzyme.

<http://www.ncbi.nlm.nih.gov/pubmed/10197050> Inhibitors of tryptase for the treatment of mast cell-mediated diseases

<http://www.ncbi.nlm.nih.gov/pubmed/12065914> Serum tryptase levels in patients with mastocytosis: correlation with mast cell burden and implication for defining the category of disease.

<http://www.ncbi.nlm.nih.gov/pubmed/2468689> Time course of appearance and disappearance of human mast cell tryptase in the circulation after anaphylaxis. *"The peak level of tryptase after an experimentally induced systemic anaphylactic reaction occurred 1-2 h after the initiating bee sting in each of three subjects, in contrast to histamine levels which peaked at 5-10 min. In some cases elevated levels of tryptase may not be detected during the initial 15-30 min. Tryptase levels then declined under apparent first order kinetics with a t1/2 of approximately 2h."*

<http://www.ncbi.nlm.nih.gov/pubmed/15025392> Effector cells of anaphylaxis: mast cells and basophils.

[http://en.wikipedia.org/wiki/Mast\\_cell](http://en.wikipedia.org/wiki/Mast_cell) Mast Cell

<http://www.sciencedirect.com/science/article/pii/S0925443910002954> Mast cell activation and autism. *"A number of papers, mostly based on parental reporting on their children's health problems, suggest that ASD children may present with "allergic-like" problems in the absence of elevated serum IgE and chronic urticaria. These findings suggest non-allergic mast cell activation, probably in response to environmental and stress triggers that could contribute to inflammation."*

<http://home.allergicchild.com/food-allergies-mast-cells-hitting-your-threshold/> Food Allergies, Mast Cells, and Hitting Your Threshold.

[http://www.nature.com/ni/journal/v8/n8/fig\\_tab/ni0807-796\\_F1.html](http://www.nature.com/ni/journal/v8/n8/fig_tab/ni0807-796_F1.html) Figure 1 - Expression of GATA-3 in the absence of Notch-DL1 signaling drives mast cell development.

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1279398/> CHARACTERISTICS OF HISTAMINE RELEASE EVOKED BY ACETYLCHOLINE IN ISOLATED RAT MAST CELLS. *"Histamine secretion from rat mast cells occurs in the presence of nanomolar concentrations of acetylcholine."*

<http://www.ncbi.nlm.nih.gov/pubmed/10864147> Characterization of histamine release induced by fluoroquinolone antibacterial agents in-vivo and in-vitro.

<http://www.ncbi.nlm.nih.gov/pubmed/10771034> Mechanism of histamine release induced by levofloxacin, a fluoroquinolone antibacterial agent.

<http://www.ncbi.nlm.nih.gov/pubmed/9635500> Histamine-releasing properties of T-3762, a novel fluoroquinolone antimicrobial agent in intravenous use. II. Dermovascular permeability-increasing effect and action on peritoneal mast cells.

<http://www.ncbi.nlm.nih.gov/pubmed/10884641> Salivary gland changes in chronic fatigue syndrome: a case-controlled preliminary histologic study. *"The one parameter that showed statistical significance was the presence of mast cells."*

<http://www.ncbi.nlm.nih.gov/pubmed/17090238> Nicotinic acetylcholine receptors on basophils and mast cells. *"Anaphylaxis in response to drugs administered during anaesthesia is a rare but potentially catastrophic event. The anaesthetic drugs most commonly associated with anaphylaxis are neuromuscular blocking agents. As these drugs act on the nicotinic acetylcholine receptor of the*

neuromuscular junction, potentiation of anaphylaxis by a **nicotinic receptor on basophils and mast cells** is plausible.”

[http://nopr.niscair.res.in/bitstream/123456789/6558/1/IJEB%2044\(8\)%20627-634.pdf](http://nopr.niscair.res.in/bitstream/123456789/6558/1/IJEB%2044(8)%20627-634.pdf) Modulation of Gastric Mucosal Mast Cell Population: Role of Vestibulo Cerebellar Lesion

<http://www.sciencedirect.com/science/article/pii/S0014579395014667> Murine and human mast cell express acetylcholinesterase. “. . . *The primary type of AChE mRNA produced by these cells was found to be the brain and muscle . . .*”

<http://onlinelibrary.wiley.com/doi/10.1111/sms.12089/abstract> **Increased mast cell numbers in a calcaneal tendon overuse model.** “*Tendinopathy is often discovered late because the initial development of tendon pathology is asymptomatic. The aim of this study was to examine the potential role of mast cell involvement in early tendinopathy using a high-intensity uphill running (HIUR) exercise model . . . The current study demonstrates that 7-week HIUR causes structural changes in the calcaneal tendon, and further that these changes are associated with an increased mast cell density.*”

<http://bjsm.bmj.com/content/early/2008/02/28/bjsm.2007.040212> **Elevated mast cell numbers in human patellar tendinosis: correlation with symptom duration and vascular hyperplasia.** “*The cellular basis of painful tendon overuse pathology (tendinosis) is poorly understood. Due to close anatomic associations between mast cells and vessels in connective tissues, it has been postulated that mast cells may mediate the development of tendon hypervascularity or edema. Therefore, the purpose of this study was to examine the distribution of mast cells in men and women with patellar tendinopathy . . . Conclusion: Mast cell prevalence in patellar tendinopathy was increased and was predominantly associated with vascular hyperplasia -- particularly among patients with longstanding symptoms. Future research should investigate whether mast cells play direct or indirect modulatory roles in the development and progression of human tendinosis.*”

<http://mastcelldisorders.wallack.us/yabb/YaBB.pl?num=1344046521> Mast Cell Disorders Forum

<http://mastcelldisorders.wallack.us/yabb/YaBB.pl> Mast Cell Disorders Forum

[http://www.foodsmatter.com/allergy\\_intolerance/histamine/articles/histamine.html](http://www.foodsmatter.com/allergy_intolerance/histamine/articles/histamine.html) Histamine

<http://meandmymastcells.com/category/the-symptoms/> Me and My Mast Cells

<http://www.autismweb.com/forum/viewtopic.php?f=4&t=32038> Autism Web Forum: Mast Cell Activation and MAO A mutation

<http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0076241> Familial Occurrence of Systemic Mast Cell Activation Disease

<http://www.evilmastcells.com/MCAD-Doctors.html> Mast Cells Disorders Doctors in the U.S.

<http://www.mastattack.org/2014/04/> Mast Attack: Educating People About Life With Mast Cell Disorders

<http://www.ncbi.nlm.nih.gov/pubmed/11517853> The suppressive mechanism of histamine release from rat peritoneal mast cells of iodine-enriched eggs. “We investigated the antiallergic activity of iodine-enriched egg by using rat peritoneal exudate cells.”

<http://cardiovascres.oxfordjournals.org/content/89/1/12> Cardiac mast cells: the centrepiece in adverse myocardial remodeling

<http://content.onlinejacc.org/article.aspx?articleid=1137962> Histamine, Mast Cells, and Heart Failure: Is There a Connection?

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## IgG4-RD/EoE

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<http://news.yahoo.com/throat-closing-ailment-eoe-mystery-must-solved-op-003551374.html> Throat-Closing Ailment EoE is a Mystery That Must Be Solved. Good article, FQ's may induce EoE and MCA? Comments are informative.

<http://wexnermedical.osu.edu/patient-care/healthcare-services/allergy-care/eosinophilic-esophagitis>  
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