Damage to receptors or enzymes with specific tyrosyl residues, tyrosine kinases or phosphatases, phosphotyrosyl bonds, or autoantibody formation to any of these. The "Tyrosine Connection"

Tyrosine, tyrosyl residues, and phosphotyrosyl bonds are important structural and functional moieties for innumerable processes throughout the body. Because of the aromatic nature of FQ's and the symptomatology which often occurs in FQ victims, I question whether FQ's might be acting as a structural analog or inhibitor of receptors, transporters, or in other binding processes involving aromatic amino acids. FQ's bind close to a functionally important and crucial tyrosine residue in the enzymes they target, and I question whether they are targeting additional enzymes with similar functionally important tyrosine residues, especially where Mg++ is a cofactor. Anything that affects tyrosine metabolism could potentially affect any structural, receptor, enzymatic, cell signaling or signal transduction reaction tyrosine is crucial for. Below I list just a few examples. I won't go into detail for all of them; I encourage everyone to review the references I'm supplying as well as do your own research.

- The FQ antibiotics bind to bacterial gyrase (topoisomerase) enzyme located close to a catalytic tyrosine in a binding pocket utilizing Mg++. The topoisomerase enzyme binds to DNA with a phosphotyrosyl bond.
- All topoisomerases form a phosphotyrosine intermediate between the catalytic tyrosine of the enzyme and the scissile phosphoryl of the DNA backbone.
- Specific tyrosines appear to be important catalytic amino acids for topoisomerases to function.
- Specific tyrosines appear to be an important highly conserved configuration in ACh binding and recognition in nicotinic and all five muscarinic subtypes.
- Specific tyrosines in an "aromatic patch" appear to be important in the AChE active site pocket.
- Tyrosyl-DNA-phosphodiesterase 1 and 2 are DNA repair enzymes that resolve topoisomerase 1 and 2 DNA adducts and mediate resistance to anti-cancer drugs that target TOPO-DNA complexes as a result. Tdp2 is Mg dependent; Tdp1 is in mitochondria also
- There are motifs around Tyr residues that are indicators of potential phosphorylation targets by protein tyrosine kinases (PTK). The PTK's are also Mg++ dependent enzymes as are almost all that use nucleoside triphosphates as substrates
- Tyrosine kinases and phosphatases are involved in signal transduction and are key regulators of normal cellular processes. Protein kinases can become mutated, or "stuck" in the "on" or "off" position in terms of regulation. A number of viruses target tyrosine kinase function during infection – which can be one possible explanation for similarities in symptoms between FQ victims and other chronic illnesses.
- The receptors and enzymes involved in the handling of glutamate pathway—specifically NMDARs, glutamate transporter, and glutamine synthase (GS)—have key tyrosine residues as targets causing subsequent function modification resulting in neuropathic pain and excitotoxicity.
- Tyrosine and tyrosyl residues are an obvious precursor and crucial part of TH formation and utilization.
- Several chemotherapeutic agents which are broad based tyrosine kinase inhibitors can cause immediate and delayed hypo and hyperthyroidism in 25% - 85% of patients who take them.
- Tyrosine is an important precursor for the neurotransmitters and catecholamines, such as dopamine, noradrenaline, and adrenaline.
- Tyrosine is known to affect metabolism of glucocorticoid hormones (GHs) and is being studied as a valid monitoring parameter for GH status and adrenal function
- Tyrosine is needed to synthesize the benzoquinone structure which forms part of coenzyme Q10.

- Tyrosine metabolism appears to be important in connective tissue disorders, with one known genetic alteration resulting in spontaneous tendon ruptures.
- Tyrosine appears to play a specialized role in collagen structure and function, including catalyzing the process of fibril formation.
- Tyrosine transporters are involved in large neutral amino acid cellular uptake (phenylalanine, tyrosine, leucine, arginine and tryptophan), T3/T4 uptake, L-Dopa uptake, are involved in neuronal cell proliferation in the brain, *play a role in metal ion homeostasis and toxicity*, and act as the major transporter of tyrosine in fibroblasts.
- Tyrosine aminotransferase and transporter activity are induced by cortisol, theophylline, caffeine, and adenine; albeit conflicting studies
- Methylxanthine binding interactions in the catalytic pocket include an important tyrosine residue; binding affinity is reinforced by a tyrosine residue
- A single specific tyrosine is highly conserved and necessary for binding in GABA transporter, playing a critical role in neurotransmitter recognition
- A single specific Tyrosine (955) is a highly conserved residue critical for nucleotide recognition among family A DNA polymerases, including pol Y within mitochondria. Sequence alignments reveal there are equivalent active site Tyrosines located in E.Coli and T7 bacteriophage.
- Tyrosinase is an important enzyme in melanogenesis and recently was reported to be linked to Parkinson's Disease and other neurodegenerative diseases. FQ's are known to inhibit tyrosinase activity.
- Tyramine oxidases (old name) = monoamine oxidases – tyramine has chemical relationship to thyroxine, L-tyrosine, and adrenaline. Consider Tyramine "flares" causing pheo-like hypertensive crises ("cheese effect").
- The insulin receptor belongs to the large class of tyrosine kinase receptors; FQ's may act as TKI's and have a long history of dysglycemias as an ADR.
- Spirochetes of the genus *Borrelia* include the tick-transmitted causative agents of Lyme disease and relapsing fever -- consider ResT enzyme of these organisms, which use a reaction mechanism similar to that of the type IB topoisomerases and tyrosine recombinases -- look for tyrosine based possibilities for pathologic mechanisms of action to humans? What part of cellular process does *Borrelia* hijack and if so, how does it do so? Look for common mechanisms of viral induced, drug (FQ) induced, and *Borrelia* induced pathology searching tyrosine-based reactions, including genomic damage.
- A number of viruses target tyrosine kinase function during infection.
- Protein tyrosine kinases, have a major role in the activation of lymphocytes.
- FQ's are able to photodamage isolated aromatic amino acids, with tyrosine being a major one.
- Participation of aromatic amino acids tyrosine (Tyr) and tryptophan (Trp) groups in drug-serum albumin complexes occurs with FQ's (Avelox)
- Tyrosine kinases and phosphatases may be a mechanism of NIS regulation, and therefore iodine uptake regulation.
- An immunoreceptor tyrosine-based inhibition motif (ITIM), is a conserved sequence of amino acids (S/I/V/LxYxxI/V/L) that is found in the cytoplasmic tails of many inhibitory receptors of the immune system. These might be important in autoimmunity or hypersensitivity functions – ie, can't turn the signal off.