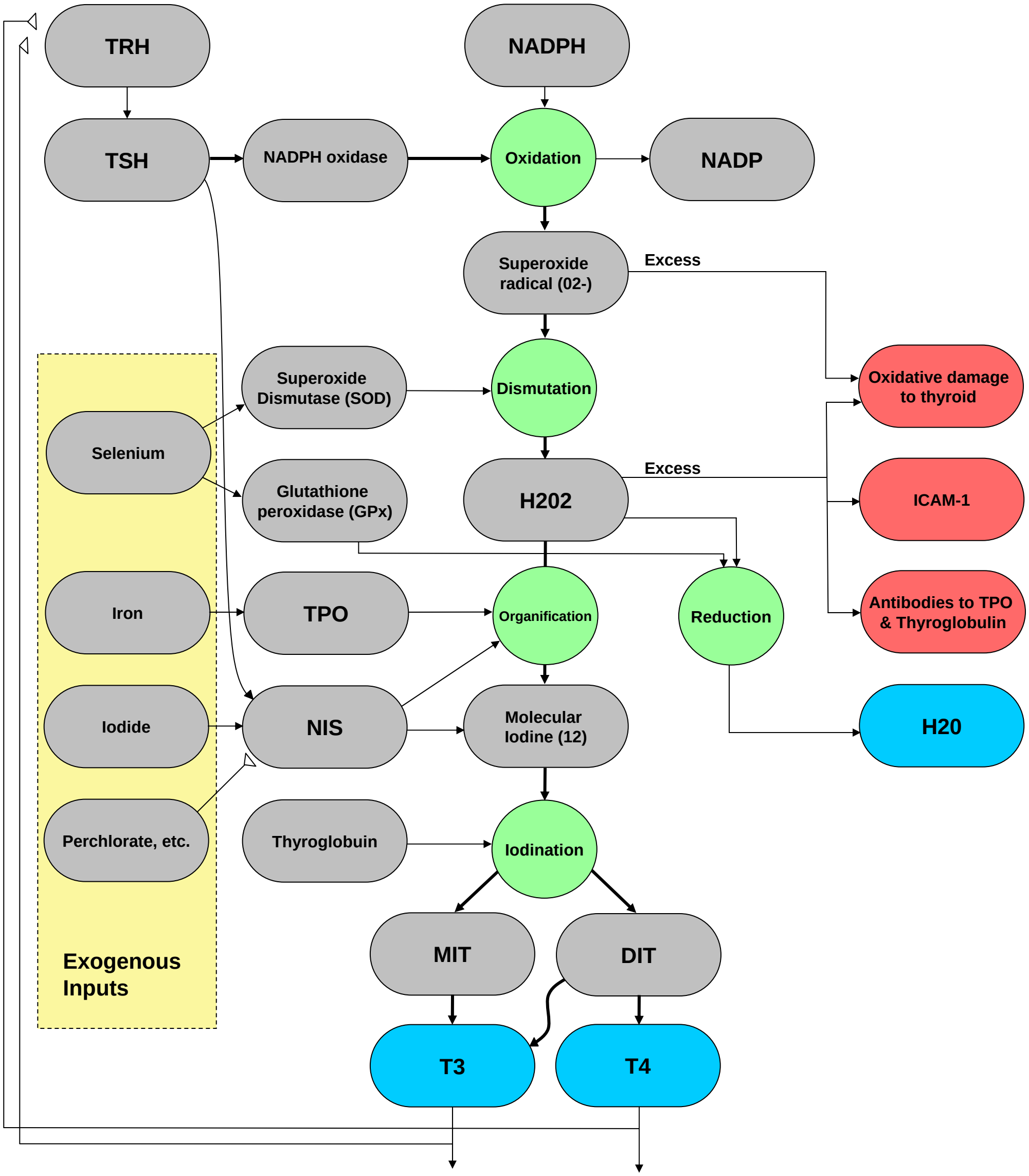
Thyroid Hormone Production



Normal process: Thyroid hormone levels drop. TSH binds to receptors on the follicular cells, stimulates NIS activity and also ensures H202 will be available as a substrate by inducing NADPH oxidase, which oxidizes NADPH to NADP, liberating superoxide radicals ($O2^{-}$), which are then converted to the less potent free radical, H202, by SOD, a selenium-dependent enzyme. NIS transports Iodide (I^{-}) into the follicular cell where it is catalyzed by heme-dependent TPO using H202 to form I2, which then binds to tyrosine residues in thyroglobulin to form MIT and DIT. DIT+ DIT then produce T4; DIT + MIT produce T3. H202 that is not used up in this process is neutralized by selenium-dependent glutathione peroxidase. *Iodine deficiency / Selenium deficiency / Iron deficiency:* Low iodine stores result in low levels of thyroid hormones, which activates TSH. H202 is produced, but no iodide arrives. If selenium is also insufficient, $O2^{-}$, a more potent ROS than H202, is formed and is not converted to H202. If iron is deficient, TPO will not be available to catalyze iodide, so H202 will remain to cause damage to the follicular cell. *Iodine repletion*: the Wolff-Chaikoff effect will prevent excessive organification of iodide; however, during the formation of thyroid hormones, some ROS will be generated in excess of those used to produce I2, and will cause damage if not reduced by glutathione peroxidase.