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MODERATE IODINE DEFICIENCY CAUSES GESTATIONAL HYPOTHYROXINEMIA IN DEHAL1 KO MICE

Pouya Alikhani[1], Andrea Bertolini[2], Eva González Iglesias[1], Abraham García López[1], María Fuentes-Andión[1], Alessandro Saba[2], Riccardo Zucchi[3], Jose Moreno[4]

[1]*Thyroid Molecular Laboratory, Institute for Medical and Molecular Genetics (Ingemm), La Paz University Hospital, Madrid, Spain*
[2]*Department of Pathology, University of Pisa, Italy*
[3]*University of Pisa, Dept. of Pathology, University of Pisa, Pisa, Italy*
[4]*Thyroid Molecular Laboratory, La Paz University Hospital, Autonomous University of Madrid, Madrid, Spain*

Gestational hypothyroxinemia is frequent in human pregnancies, being attributed to environmental iodine deficiency (ID). However, iodine supplementation in countries with moderate ID seems insufficient to fully eradicate the disorder. Dehal1 is the enzyme that recycles iodide in the thyroid through deiodination of mono- and di-iodotyrosines (MIT, DIT). We hypothesised a combined environmental-genetic etiology for gestational hypothyroidism and tested such model *in vivo* using *Dehal1* knockout (KO) mice.

Objective To determine the effects of moderate nutritional ID combined with the lack of iodide-recycling on thyroid hormone levels during mouse pregnancy.

Materials & Methods From mating, female wild type (WT) and *Dehal1* KO mice were fed with normal (NID: 5.8 µg I/day) or moderately low (LID: 0.8 µg I/day) iodine diets throughout pregnancy. Plasma was collected before conception (day0) and after delivery (day 21), and urine also at mid-gestation (day10). Plasma T4 and T3 and urinary MIT and DIT were measured using LC/MS-MS. Urinary iodide concentration (UIC) was determined by Sandel-Kolthoff. The t-test was used for statistical analysis.

Results Plasma T4 at the end of pregnancy was only decreased in KO mice under LID (Table). T3 remained similar among and within experimental groups. UIC increases at midgestation under NID, but not under LID, in both genotypes. Iodotyrosines were not detectable (*n.d.*) in the urine of WT mice. However, in KO mice both MIT and DIT were measurable and increased significantly at midgestation, most remarkably under NID diet (** compared to baseline within each group; # compared to values in WT-NID;* * p<0.05, ** p<0.01, *** p<0.001).

		T4 *ng/ml*	**T3** *ng/ml*	**UIC** *µgI/mg creat.*	**MIT** *ng/ml*	**DIT** *ng/ml*
WT-NID	Day0	29.5	0.4	5.1	*n.d.*	*n.d.*
	Day10	-	-	**9.2 ***	*n.d.*	*n.d.*
	Day21	42.9	0.8	5.1	*n.d.*	*n.d.*
WT-LID	Day0	29.5	0.4	5.1	*n.d.*	*n.d.*
	Day10	-	-	3.37	*n.d.*	*n.d.*
	Day21	34.5	0.7	7.93	*n.d.*	*n.d.*
KO-NID	Day0	32	0.4	**10.9** #	3.31	1.76
	Day10	-	-	**58.7 *** **	**10.17 *** **	**6.52 ** **
	Day21	39.5	0.8	**35.2 *** **	**8.1****	3.44
KO-LID	Day0	32	0.4	10.9 #	3.31	1.76
	Day10	-	-	**2.8 *** **	**5.11 ***	3.48
	Day21	**24.4 *** **	0.6	**6.1 ***	3.06	2.06

Conclusion Moderate ID during pregnancy causes hypothyroxinemia only when the iodide-recycling capacity is defective in mice. This supports a bi-factorial model for gestational hypothyroxinemia in mammals, including nutritional and genetic deficiencies, that could be hallmarked by iodotyrosines.

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