Dirty jobs...

Occupational COPD and HMOX1 repeats in a Danish population

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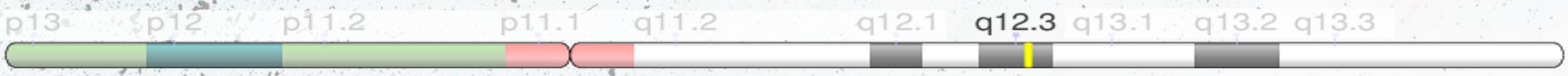


Chr. 22 HMOX1

Credit: Genome Decoration Page/NCBI

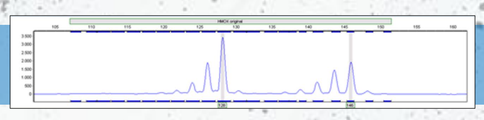
Background

- Dinucleotide repeats $(GT)_n$ in the heme oxygenase 1 (HMOX1) gene modulate the gene expression.
- Long repeats might affect COPD occurrence.

Aim

- Investigate associations of the HMOX1 polymorphism of $(GT)_n$ repeats to occurrence of COPD.

Methods



- Population based cohort: N=4703 Danes of Northern European descent, aged 45-84.
- COPD: Defined by LLN 2.5th FEV_1/FVC and FEV_1 centiles.
- Occupational exposure: Cumulated years (0, <5, 5-14, ≥15) worked with vapour, gas, dust or fume (VGDF) exposure.
- HMOX1: Genotyped by fragment analysis and capillary electrophoresis, and grouped according to short (S): ≤26, medium (M): 27-32 and long (L): ≥33 GT repeat alleles in an L dominant genetic model.
- Analysis: Mixed random effect logistic regression adjusted for smoking, sex, occupational exposure, age and general practitioner practice.

Results

- 6% had COPD.
- 48% had smoked ≥10 pack-years.
- 46% had an occupational VGDF exposure.
- HMOX1 $(GT)_n$ genotype was present in 4423 participants, **Table 1**.
- Crude association between COPD and HMOX1 with at least one long GT repeat (S/L, M/L, L/L) GT genotype was OR 1.66 (95% CI: 1.17-2.34).
- Adjusted results: Parts of all variables were significantly associated to COPD, **Table 2**.
- A Significant interaction was seen between HMOX1 long GT genotype and ever occupational exposure, OR 2.38 (95% CI: 1.04-5.46).

TABLE 1:
HMOX1 dinucleotide repeat genotypes

	n GT repeats	Study n=4423 n	Study n=4423 %	Replication n=1082 n	Replication n=1082 %
S/S	≤26	534	12	141	13
S/M		1875	42	443	41
M/M	27-32	1547	35	361	33
S/L		172	4	46	4
M/L		289	7	86	8
L/L	≥33	6	0.1	5	0.5

TABLE 2: Associations to COPD

		Study OR	Study 95% CI	Replication OR	Replication 95% CI
VGDF exposure	No	Ref.	-	Ref.	-
	<5(yes)	1.11	0.64-1.92		
	5-14 (yes)	**1.62**	1.02-2.56	1.73	0.73-4.09
	≥15 (yes)	1.38	0.98-1.95		
HMOX1	S/S, S/M, M/M	Ref.	-	Ref.	-
	S/L, M/L, L/L	**1.74**	1.17-2.59	0.23	0.03-1.74
Smoked pack-years	<10	Ref.	-	Ref.	-
	10-20	**2.68**	1.57-4.59	2.59	0.95-7.04
	>20	**7.66**	5.13-11.41	**3.59**	1.29-10.00
Age	20-25	-	-	Ref.	-
	26-30	-	-	1.02	0.26-3.99
	31-35	-	-	0.50	0.11-2.33
	36-40	-	-	0.89	0.24-3.29
	41-47	-	-	0.87	0.23-3.30
	45-54	Ref.	-	-	-
	55-64	1.28	0.76-2.17	-	-
	65-74	**2.24**	1.40-3.58	-	-
	75-84	**2.32**	1.38-3.91	-	-
Sex	Female	Ref.	-	Ref.	-
	Male	**0.54**	0.37-0.79	1.68	0.73-3.86

Replication

- Younger Danish cohort "RAV", aged 20-44 and born in Scandinavia, N=1168.
- 3% had COPD.
- 25% had smoked ≥10 pack-years.
- 20% had an occupational VGDF exposure, used as a dichotomised variable.
- HMOX1 $(GT)_n$ genotype was present in 1082 participants, **Table 1**.
- Crude association between COPD and the long GT genotype was insignificant and rather protective, OR 0.45.
- Adjusted results: Only smoking >20 pack-years was associated to COPD, **Table 2**.
- No variables showed a significant interaction with the HMOX1 long GT genotype.

Conclusion

- **Findings in the elderly cohort supports an association between occupational exposure and COPD with HMOX1 repeats in the model and long GT repeat in HMOX1 seems to interact with environmental exposure but not with smoking.**
- **Failure to replicate data in the young cohort might be due to premature age for development of COPD and low prevalence of occupational exposure.**

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