Clonal Hematopoiesis in Inflammatory Bowel Diseases

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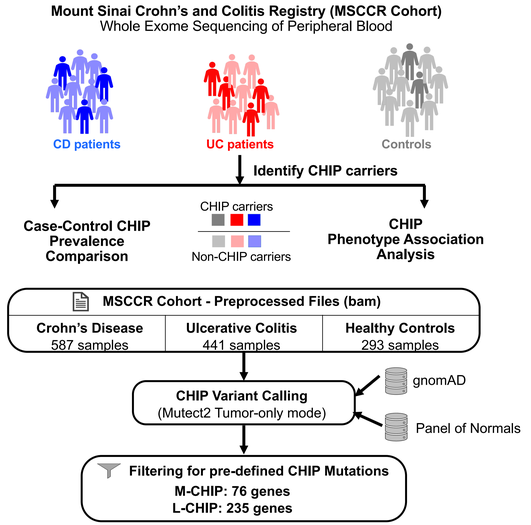
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BACKGROUND

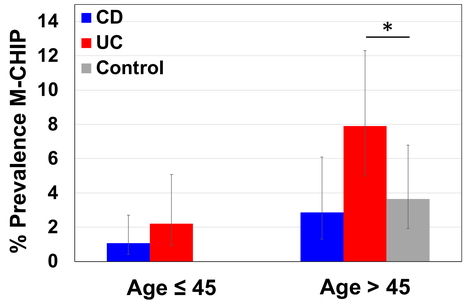
- Clonal hematopoiesis (CH) is the age associated expansion of somatic mutations in hematopoietic stem and progenitor cells.
- CH at >2% variant allele frequency (VAF) in the absence of hematologic disease defines clonal hematopoiesis of indeterminate potential (CHIP).
- CHIP is associated with inflammatory diseases.
- Inflammatory bowel disease (IBD) is characterized by systemic inflammation and may represent a novel risk factor for CHIP.
- CHIP has previously been investigated in ulcerative colitis (UC) but not in Crohn's disease (CD) or compared to controls in either UC or CD.

METHODS

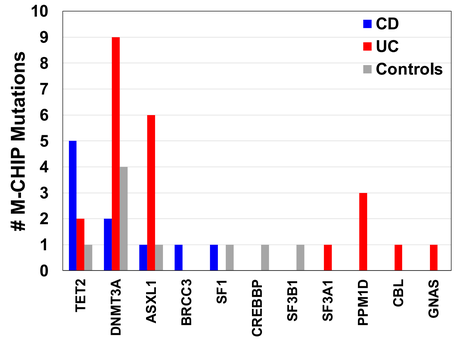


RESULTS

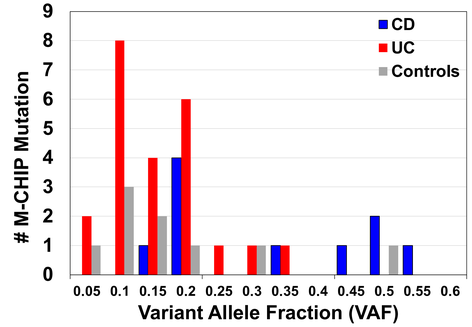
Older UC patients had significantly higher prevalence of CHIP compared to controls (OR=2.3 95% CI = 1.0– 5.2, p = 0.05)



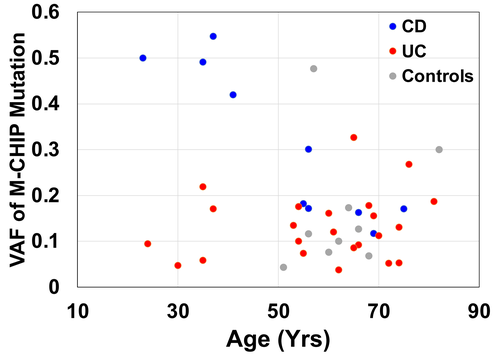
DNMT3A, ASXL1, TET2, and PPM1D were the most frequent CHIP genes in UC and TET2 and DNMT3A were common in CD



Patients with CD had higher observed VAF than patients with UC and controls



Younger age was associated with higher VAF in patients with IBD (OR=0.15, 95% CI = 0.03 – 0.75, p = 0.02)



In patients with IBD, disease severity, comorbid autoimmune disease, malignancy, of history of thrombosis were not significant risk factors for the presence of CHIP

Covariate		All IBD (N = 1028) CHIP Negative N (%)	CHIP Positive N (%)	OR	P value
Antibiotics	No	715 (73)	36 (77)	0.821	0.576
	Yes	266 (27)	11 (23)		
Neutropenia	No	498 (87)	22 (85)	1.176	0.771
	Yes	77 (13)	4 (15)		
TPN Use	No	892 (91)	42 (89)	1.279	0.613
	Yes	83 (9)	5 (11)		
Harvey Bradshaw Index	Active	165 (29)	6 (32)	0.887	0.811
	Remission	403 (71)	13 (68)		
Autoimmune Disease	No	833 (85)	40 (85)	0.985	0.971
	Yes	148 (15)	7 (15)		
Malignancy	No	582 (89)	27 (87)	1.150	0.800
	Yes	75 (11)	4 (13)		
Thrombosis	No	969 (99)	47 (100)		
	Yes	12 (1)	0 (0)		

SIGNIFICANCE

- CHIP is observed at high rates in patients with IBD when compared with a control population.
- UC is more of a risk for CHIP at older age than CD.
- High VAF clones were observed in young patients with CD.
- Screening programs may be considered for IBD patients with other traditional CHIP risk factors.

ACKNOWLEDGEMENTS

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