The association of blood-borne microparticles and neutrophil activation with decompression sickness

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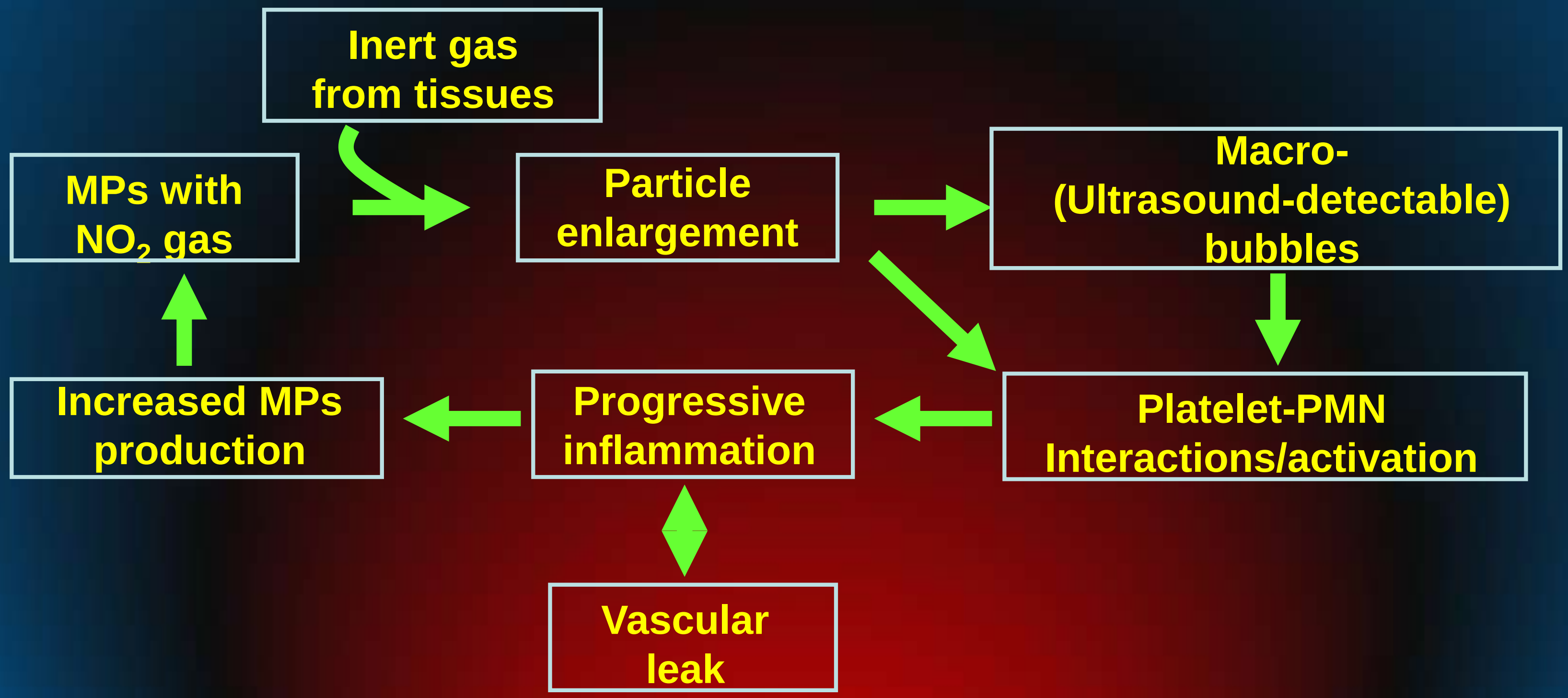
Circulating microparticles (MPs) appear to cause some of the insults following decompression stress. MPs are elevated in animals and humans after simulated or *bona fide* underwater diving.

Data supporting a relationship between MPs, neutrophil activation & DCS in human divers are lacking



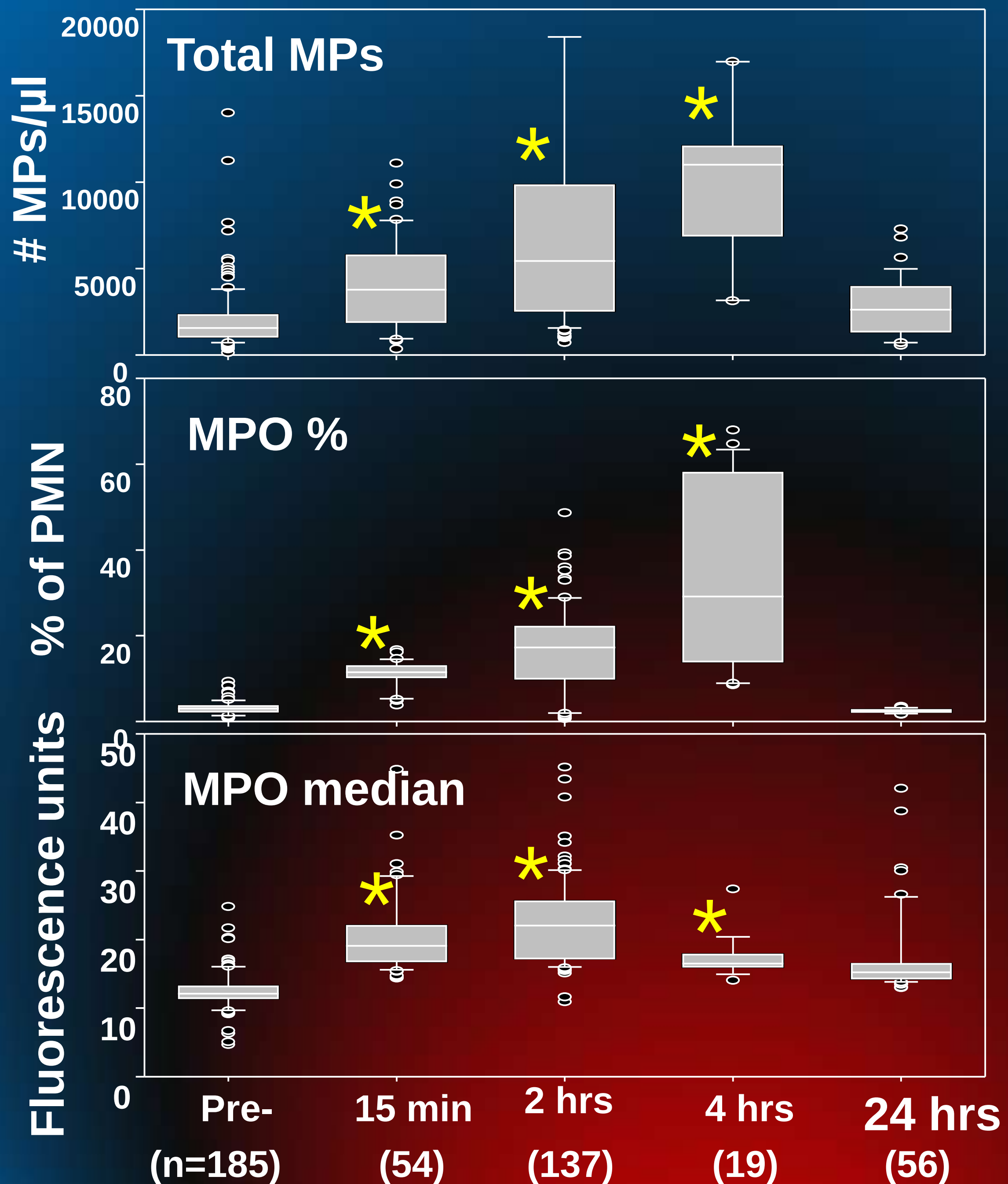
DCS = Pt. presents with S/S that improve with recompression tx.

EAN = 32% O_2/68% N_2

Tri-mix = 7-22% O_2 / 40-60% N_2 / 5-35% He

	DCS (90)	Research Subjects (185)
Age (years, median, 25th & 75th % ile)	34 (27, 42.3) Range: 16 - 73	40 (37, 44) Range: 21 - 72
Dive depth (meters)	22 (16, 34)	18 (18, 33)
# Female	23 (34%)	30 (20 %)
Compressed air	69 (76.7%)	130 (70.3%)
EAN use	19 (21.1%)	28 (15.1%)
Tri-mix use	2 (2.2%)	27 (14.6%)*

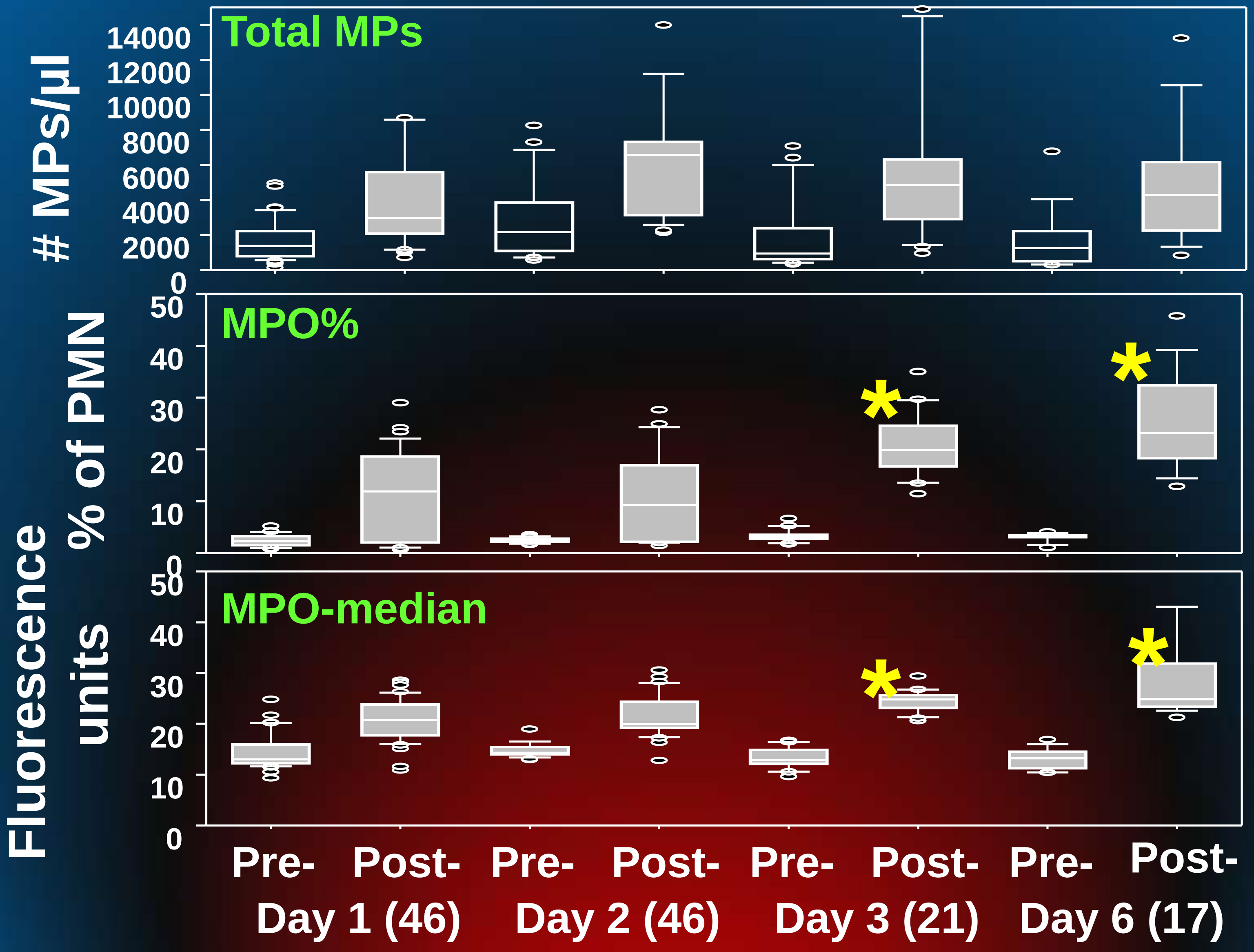
MPs & neutrophil activation occur in normal divers



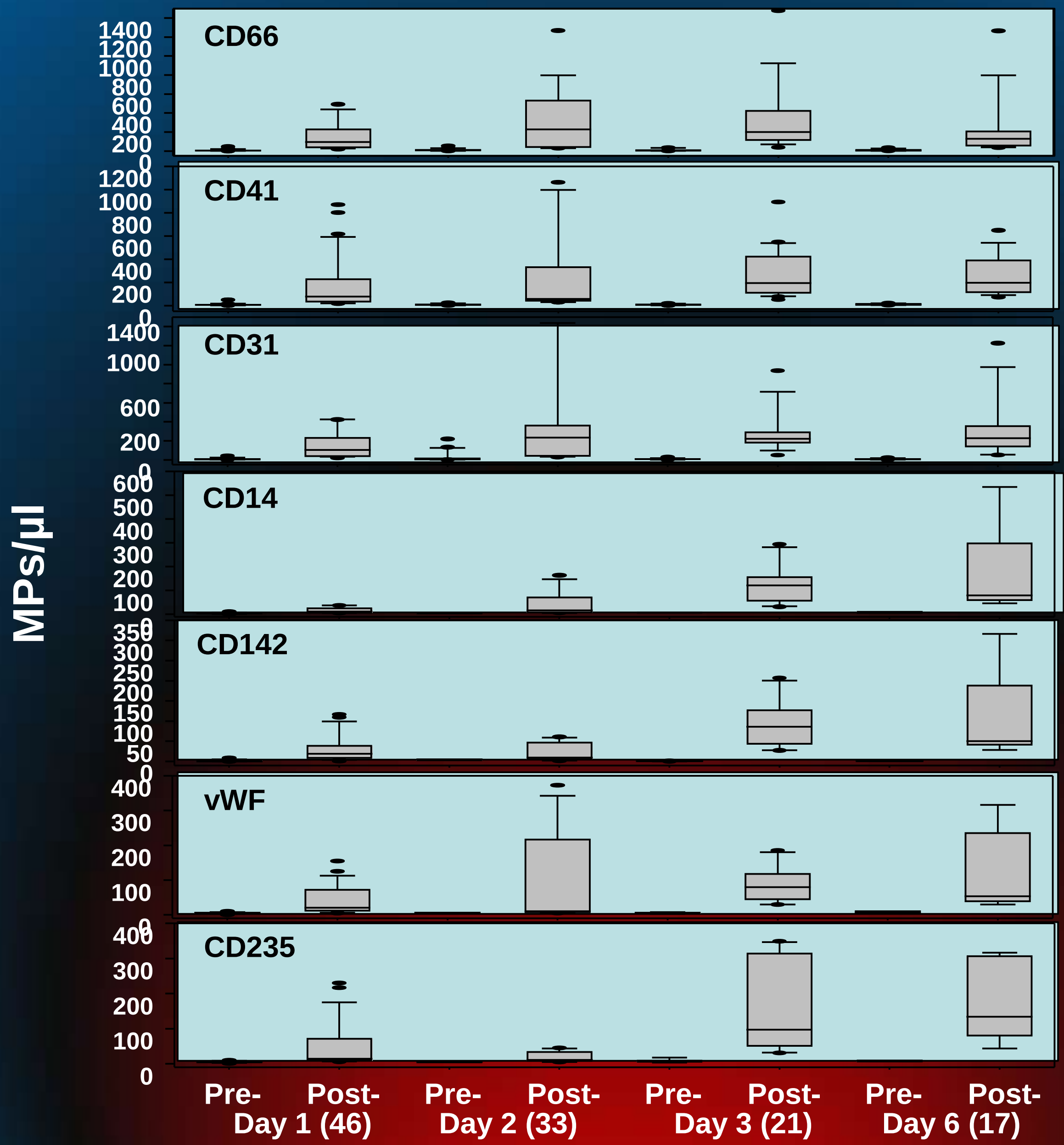
Data shown are median, 25th & 75th %ile, 10th & 90th %ile, & outliers

No significant differences based on gas or diving depth (18 – 105 msw)

Repetitive diving yields similar pattern (normalize by 24 hours)
… but with PMN activation see increase (* 2-way RM ANOVA)



Repetitive diver MPs sub-groups follow same pattern as total MPs



	Pre-dive Research subjects (185)	Post-dive Research Subjects (n=162)	DCS Divers-Acute (n=90)	DCS Divers-f/u (n=35) 28 days (13.5-35) Post-tx
Total MPs/µl	1448 (946, 2165)	2391 (1258, 5123)*	2716 (945, 6920)*	2047 (779, 3682)
MPO %	2.6 (1.9, 3.5)	5.8 (2.7, 12.2)	11.5 (4.3, 24.4)*	10.3 (4.6, 18.3)*
MPO-median	12.2 (11.4, 14.0)	15.3 (13.5, 21.6)*	16.4 (13.8, 19.9)*	14.9 (12.8, 22.3)
MPs-CD66b/µl	4.8 (1.8, 38.2)	31.1 (15.9, 44.3)*	84.0 (22.8, 148.9)*†	55.7 (18.8, 128.9)*
MPs-CD41/µl	9.6 (4.5, 33.7)	45.0 (18.4, 87.5)*	110.4 (52.2, 400.9)*†	88.2 (19.5, 337.4)*
MPs-CD31/µl	13.1 (5.3, 64.2)	37.9 (21.0, 242.8)*	186.9 (70.3, 606.3)*†	137.6 (53.5, 298.3)* †
MPs-CD142/µl	1.4 (0.3, 16.9)	16.4 (2.1, 132.3)*	66.7 (24.5, 194.6)*†Δ	19.4 (8.1, 46.9)*
MPs-CD235/µl	6.4 (3.9, 15.8)	32.5 (9.0, 126.7)*	385.9 (56.6, 692.6)*†Δ	73.4 (34.1, 248.6)* †
MPs-vWF/µl	6.5 (4.0, 18.0)	38.2 (6.6, 148.3)*	248.9 (36.0, 558.0)*†Δ	58.1 (4.1, 272.0)*
MPs-CD14/µl	7.7 (4.1, 18.0)	25.5 (6.2, 81.8)*	271.2 (101.4, 765.0)*†	206.6 (26.5, 309.1)* †

Multiple logistic regression – Odds ratios, 95% confidence limits

Adjustment	MPO%	MPOm	CD66	CD41	CD31	CD142	CD14	CD235	vWF
Unadjusted	1.6 (1.2, 2.0) $p<0.001$	6.9 (2.1, 23.1) $p=0.001$	1.4 (1.2, 1.8) $p<0.001$	1.5 (1.2, 1.8) $p<0.001$	1.7 (1.4, 2.2) $p<0.001$	1.4 (1.2, 1.7) $p<0.001$	2.0 (1.4, 2.7) $p<0.001$	1.6 (1.3, 2.2) $p<0.001$	1.7 (1.3, 2.3) $p<0.001$
Time blood sample obtained	1.6 (1.2, 2.1) $p<0.001$	7.2 (2.1, 24.8) $p=0.002$	1.7 (1.3, 2.1) $p<0.001$	1.7 (1.4, 2.2) $p<0.001$	2.1 (1.6, 2.8) $p<0.001$	1.9 (1.5, 2.4) $p<0.001$	2.2 (1.5, 3.1) $p<0.001$	2.2 (1.5, 3.2) $p<0.001$	2.1 (1.5, 3.0) $p<0.001$
Diver Age	1.6 (1.2, 2.1) $p<0.001$	8.6 (2.4, 31.5) $p=0.001$	1.4 (1.1, 1.7) $p=0.005$	1.4 (1.2, 1.6) $p<0.001$	1.6 (1.3, 2.1) $p<0.001$	1.4 (1.2, 1.7) $p<0.001$	2.0 (1.4, 2.9) $p<0.001$	1.6 (1.2, 2.2) $p=0.003$	1.7 (1.2, 2.4) $p=0.001$
Time, depth, gas, repeat dive, age	1.6 (1.2, 2.1) $p=0.001$	7.1 (1.8, 27.8) $p=0.005$	1.5 (1.2, 2.0) $p=0.003$	1.6 (1.2, 2.1) $p<0.001$	2.2 (1.6, 3.1) $p<0.001$	2.0 (1.5, 2.6) $p<0.001$	3.4 (1.8, 6.4) $p<0.001$	2.4 (1.4, 4.1) $p=0.001$	2.5 (1.5, 4.2) $p<0.001$

Spearman Correlation Analysis

	MPO%	MPOm	CD66b	CD41	CD31	CD142	CD14	CD235	vWF
DCS	0.38 <0.0001	0.19 <0.01	0.28 <0.0001	0.29 <0.0001	0.41 <0.0001	0.33 <0.0001	0.46 <0.0001	0.43 <0.0001	0.42 <0.0001
MPO%		0.41 <0.0001	0.26 <0.0001	NS	0.30 <0.0001	0.25 <0.01	0.54 <0.0001	0.32 <0.0001	0.53 <0.0001
MPOm			0.23 <0.01	0.14 <0.0001	0.21 0.01	0.26 <0.01	0.44 <0.0001	0.35 <0.0001	0.59 <0.0001
CD66b				0.70 <0.0001	0.69 <0.0001	0.78 <0.0001	0.76 <0.0001	0.61 <0.0001	0.74 <0.0001
CD41					0.80 <0.0001	0.73 <0.0001	0.78 <0.0001	0.71 <0.0001	0.80 <0.0001
CD31						0.72 <0.0001	0.70 <0.0001	0.88 <0.0001	0.87 <0.0001
CD142							0.73 <0.0001	0.66 <0.0001	0.78 <0.0001
CD14								0.74 <0.0001	0.82 <0.0001
CD235									0.79 <0.0001

No correlation between DCS & diving depth, repetitive dive, gender; age negatively correlated -0.25, $p<0.0001$

CONCLUSIONS

1. MPs elevations & PMN activation occur with diving, but no difference in response based on diving depth.

2. Repetitive diving augments neutrophil activation.

3. Divers with DCS exhibit higher MPs counts and PMN activation than asymptomatic divers.

4. Statistically significant associations exist between MPs, PMN activation and DCS. But gas & repetitive diving have no meaningful impact on associations.

5. DCS divers either exhibit persistent PMN activation and MPs elevations long after tx, (possible if MPs clearance were perturbed)… Or - What we perceive as ‘elevations’ are actually baseline values for an ‘at-risk’ population.

6. Overall, findings with divers are consistent with murine model.

7. Gender does not influence DCS risk.

8. Age is a good thing for DCS risk !!

Are MPs a response to gas pressure – or to decompression?

What about bubbles ? Are MPs a nucleation site ?

Can interventions that alter MPs in murine studies diminish risk of provocative diving?