

Chronic HIV Infection Impairs the Non-Opsonic Phagocytosis of Malaria Parasites

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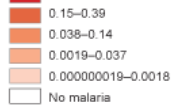
HIV and Malaria - Yes I should care!



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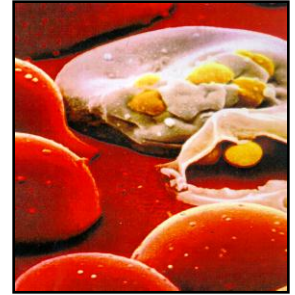
Malaria



(travellers!!)



Malaria is more severe in HIV+ individuals

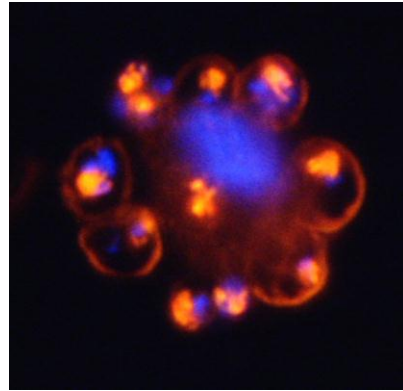
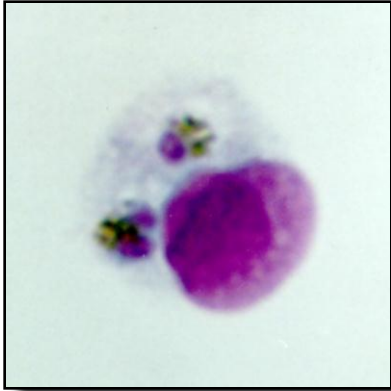


- HIV+ individuals (especially those with no immunity to malaria) are more likely:
 - to get infected with malaria
 - **to have higher parasitemia**
 - to experience more clinical and severe malaria → **more likely to die**
- Mechanisms responsible for these pathological interactions remain unclear.

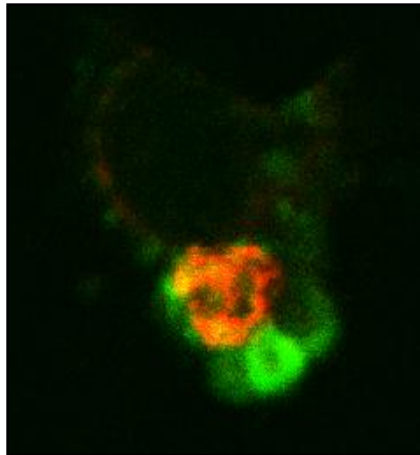
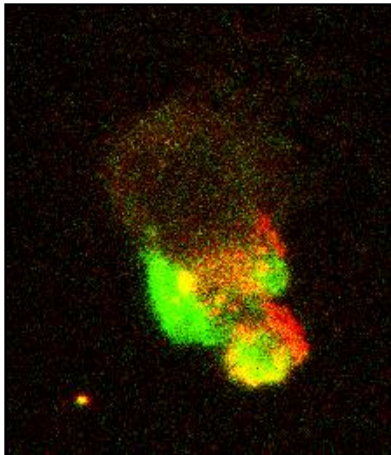
HIV impairs monocyte and macrophage function

- Impaired mono/mac effector functions have been reported in HIV infection including impaired phagocytosis of bacteria, fungi, and parasites
- These defects contribute to the morbidity and mortality associated with opportunistic infections in HIV+ individuals

Monocytes and macrophages are the first line of defence against malaria parasites



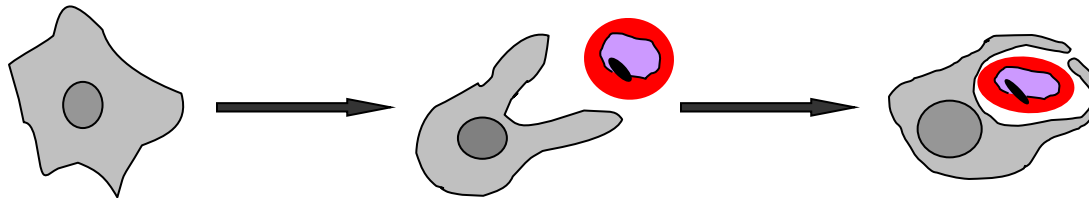
- Innate phagocytic clearance of parasites provides an early control of parasitemia



- CD36 is a major innate, non-opsonic phagocytic receptor for malaria parasites

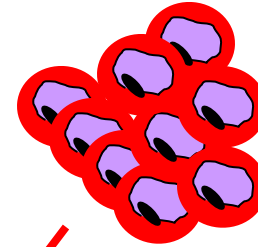
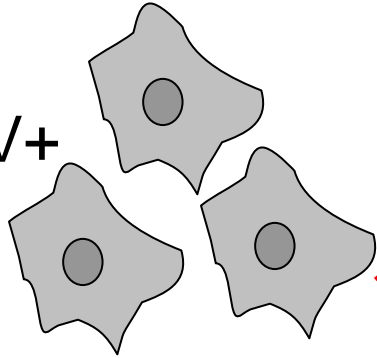
Question – Why higher parasitemia?

- Does HIV infection alter phagocytic capacity for malaria parasites?
- Does ARV therapy have an impact on this phagocytic capacity?

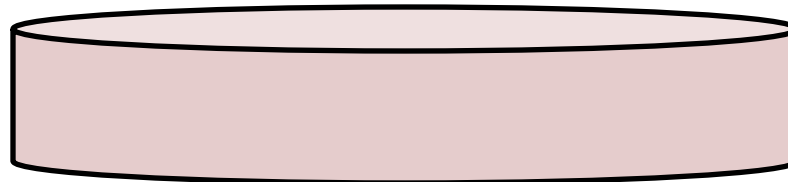


Methods: Phagocytosis Assay

Monocytes
from
chronic HIV+
or HIV-
donors



P. falciparum
parasitised
erythrocytes



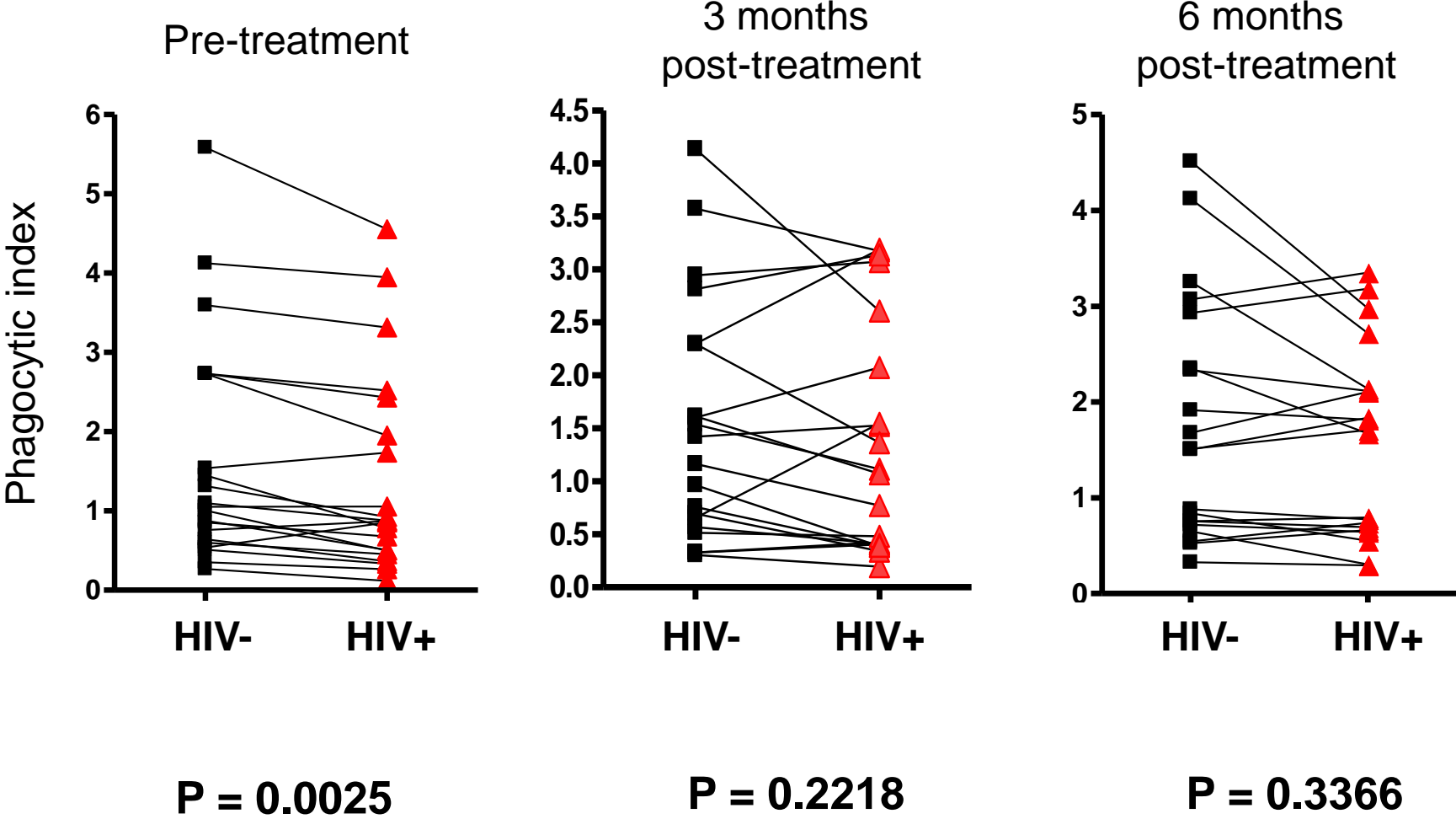
Assay performed
pre-treatment,
at 3 months and
at 6 months post-
treatment

Incubate 3hrs.
Lyse non-internalised parasites.
Fix and stain.
Quantify microscopically.

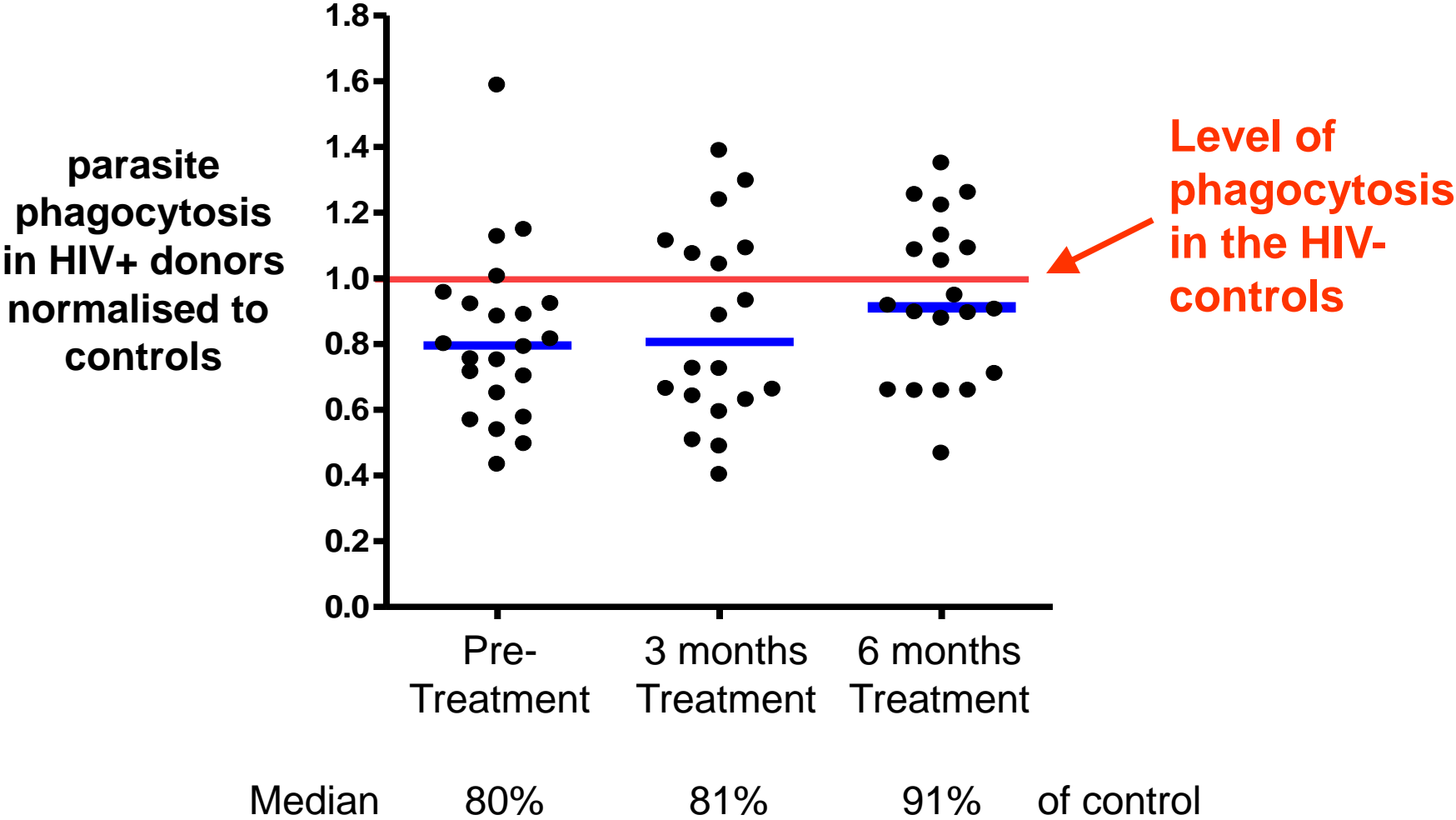
	CD4			Viral load		
	Month 0	Month 3	Month 6	Month 0	Month 3	Month 6
Donor 1	351.	378.	451.	41900.	<50	<50
Donor 2	316.	355.	454.	12929.	<50	<50
Donor 3	300.	385.	498.	190000.	<50	<50
Donor 4	290.	540.	370.	19721.	<50	<50
Donor 5	270.	400.	520.	162217.	<50	<50
Donor 6	230.	410.	480.	1102.	<50	<50
Donor 7	360.	700.	530.	426520.	<50	387
Donor 8	211.	429.	318.	183000.	<50	<50
Donor 9	320.	410.	420.	107467.	102	49
Donor 10	280.	550.	650.	7281.	108	85
Donor 11	430.	520.	680.	25632.	<50	<50
Donor 12	250.	340.	370.	57585.	<50	<50
Donor 13	290.	380.	440.	154445.	<50	<50
Donor 14	290.	330.	260.	2894.	<50	<50
Donor 15	350.	280.	260.	127074.	<50	52
Donor 16	170.	218.	260.	130000.	<50	<50
Donor 17	322.	407.	323.	337000.	<50	<50
Donor 18	272.	474.	308.	21300.	<50	<50
Donor 19	458.	541.	1274.	282000.	153	<50
Donor 20	132.	139.	212.	106000.	<50	<50
Donor 21	277.	529.	555.	72100.	241	<50
Donor 22	329.	751.	701.	732000.	175	<50
Median	295	403.5	445.5	100050	<50	<50

**Donor CD4
and viral
load data**

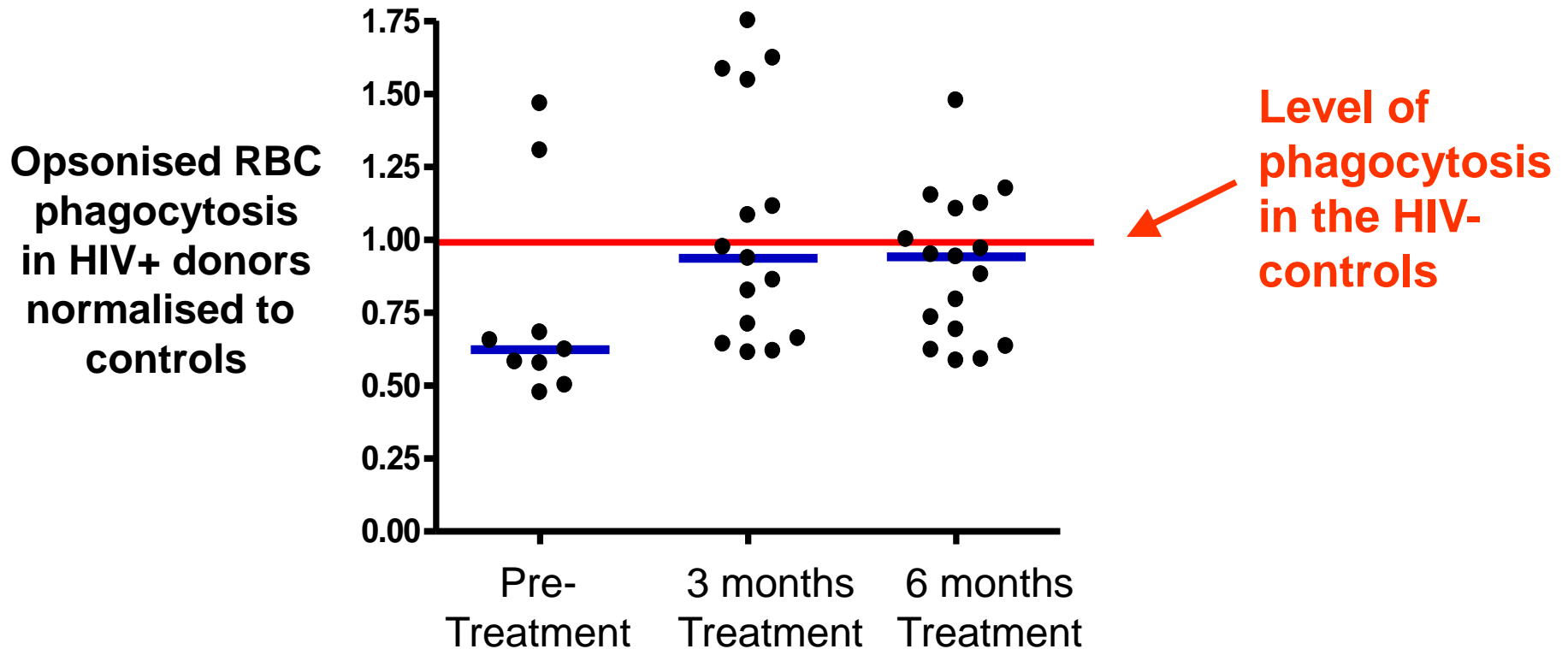
Non-opsonic phagocytosis of malaria parasites is impaired in chronic HIV+ donors but improves with ARV treatment



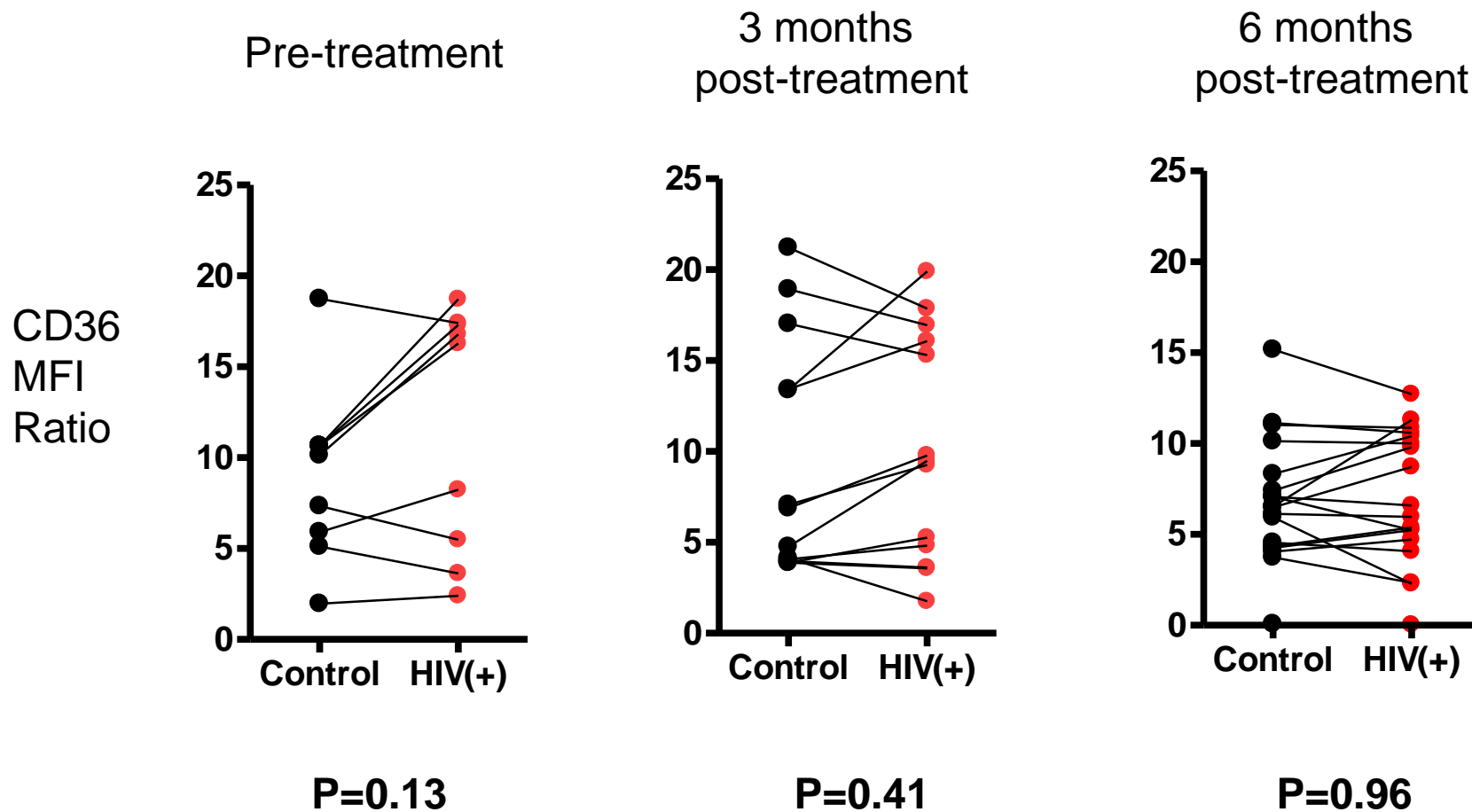
Non-opsonic phagocytosis of malaria parasites is impaired in chronic HIV+ donors but improves with ARV treatment



Opsonic phagocytosis is also impaired but recovers quicker with treatment



Monocyte CD36 levels: similar between HIV+ and controls



Summary

- Monocytes from HIV+ donors show a defect in their ability to phagocytose non-opsonised malaria parasites
- This impairment is corrected following 6 months of treatment

Conclusions

- These data may partially explain the higher parasitemia levels observed in HIV+ malaria infected patients
- Support the use of antiretroviral therapy to improve malaria outcome

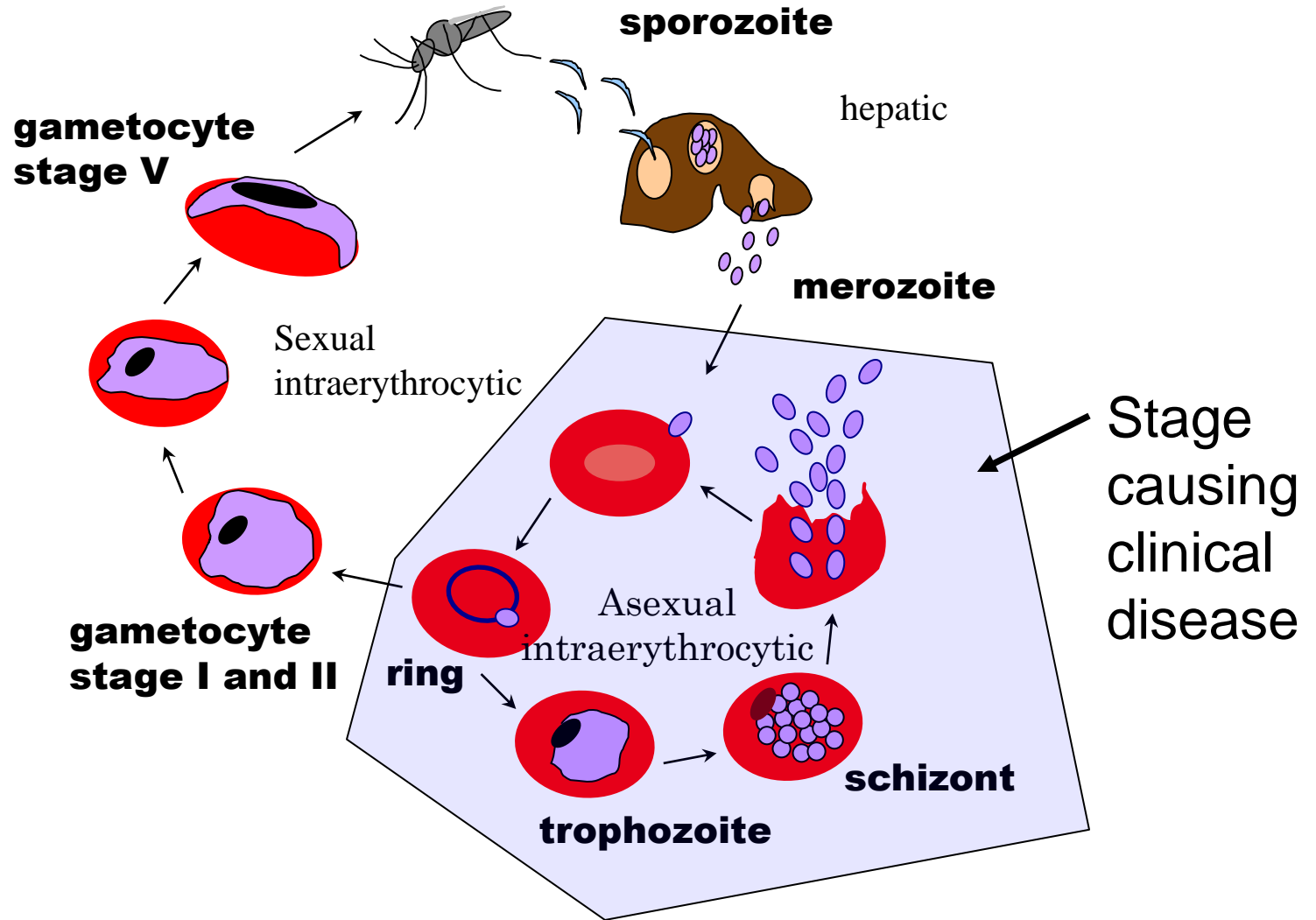
Acknowledgements

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- James Wasmuth
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- Roberta Halpenny
- All our donors

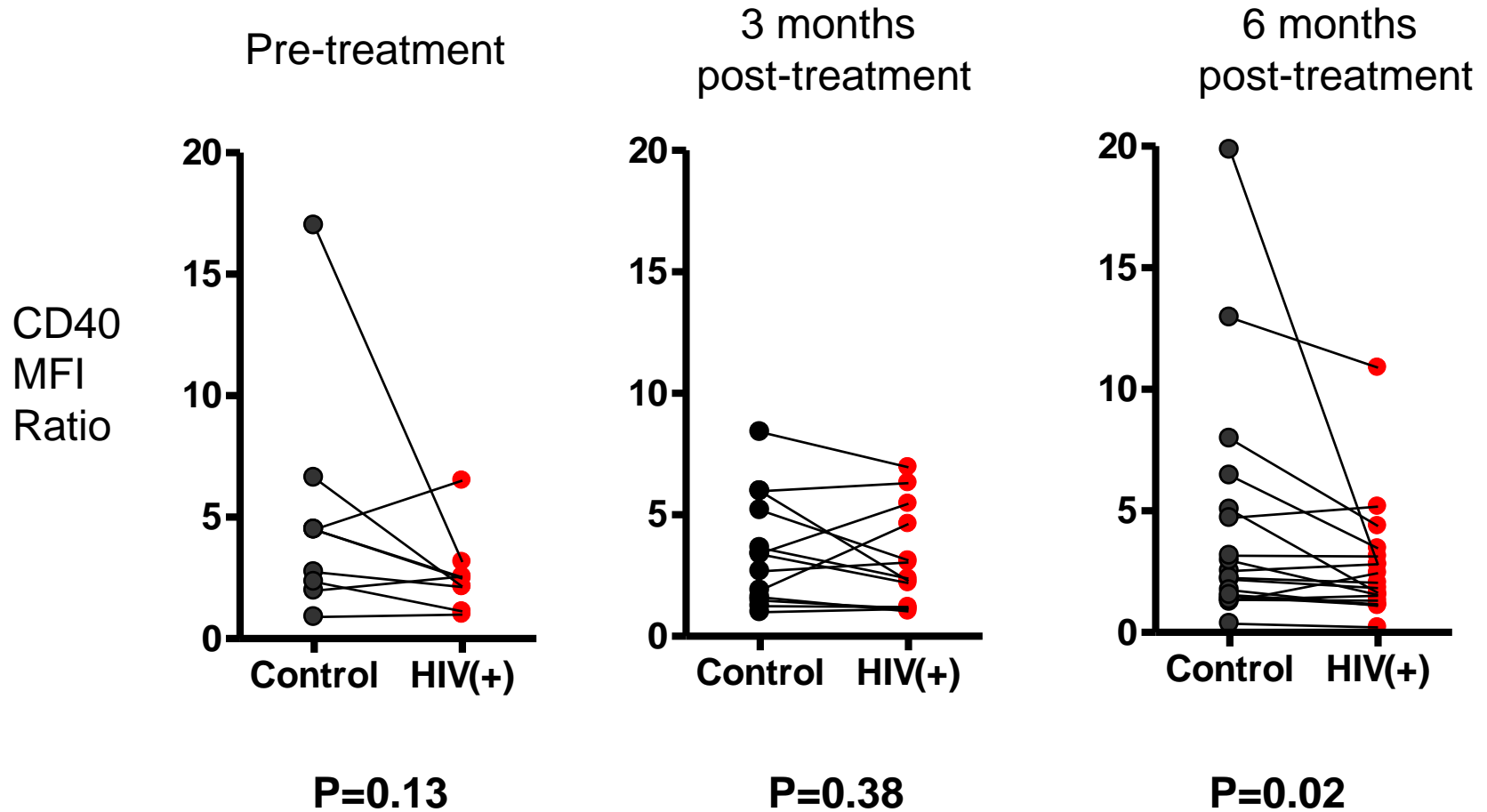
Thank you!



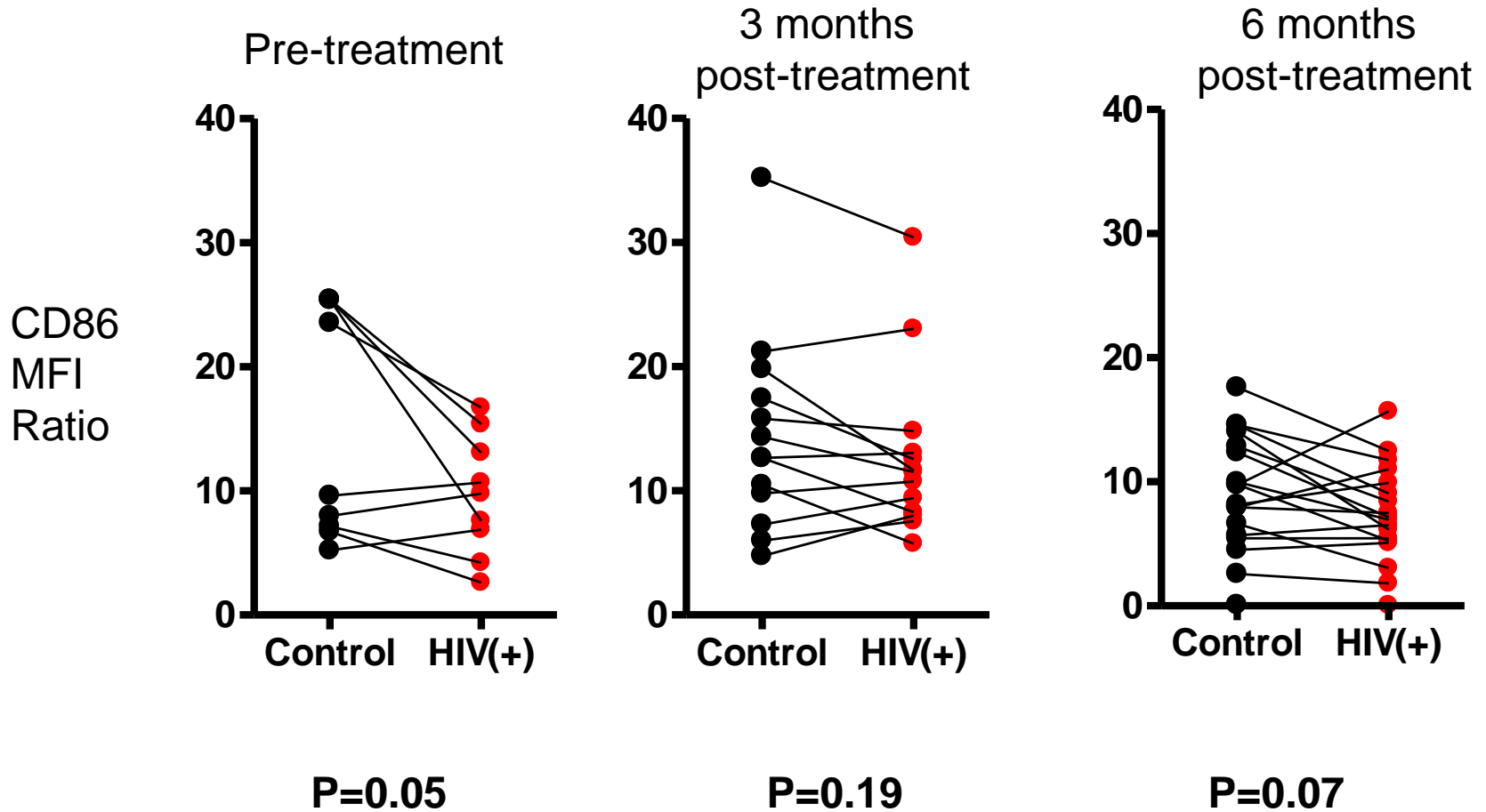
Malaria life cycle in humans



Monocyte CD40 levels: trend for lower in HIV+



Monocyte CD86 levels: trend for lower in HIV+



Monocyte HLA-DR levels: similar between HIV+ and controls

