

CURRICULUM VITAE

Alex Sigal, Ph.D.

PROFESSIONAL SUMMARY

I am interested in emerging and re-emerging viral infections, how they evolve and how they manipulate infected cells. Specific research areas include how persistent infections in immunosuppressed individuals lead to viral evolution.

EXPERIENCE

Associate Professor and Principal Investigator/Faculty at the Africa Health Research Institute and University of KwaZulu-Natal (12/2012 – present).

Max Planck Research Group Leader (seconded to Africa Health Research Institute), Max Planck Institute for Infection Biology in Berlin, Germany (12/2012 – 7/2020).

Associate Member at the Centre for the AIDS Programme of Research in South Africa (7/2020 – present).

The initial core support for my laboratory came from a position and associated funding with the Max Planck Society. I was successfully awarded two competitive renewals of the Max Planck Research Group Leader position, the maximum allowed. Funding from the position as well as grants from the NIH, the Bill and Melinda Gates Foundation, Wellcome Trust and others, allowed me to set up and run a research program combining mechanistic science and cohort based human immunology studies at the Africa Health Research Institute (AHRI, formerly K-RITH). I oversaw lab direction and re-directed funding to pivot to Covid-19 work.

MAJOR RECENT ACCOMPLISHMENTS

Covid-19 advances

- First laboratory globally to report on the escape of the Omicron variant from vaccine mediated immunity and isolate live Omicron BA.1.
- First to isolate the live Beta variant and Omicron BA.2.86 subvariant and among the first to report on the Beta and BA.2.86.
- First to report on SARS-CoV-2 evolution of immune escape from neutralizing antibodies in an individual immunosuppressed because of advanced HIV disease, a possible mechanism for how SARS-CoV-2 variants evolved.

HIV and TB advances

- Showed the role of aggregation of *Mycobacterium tuberculosis* bacilli in defeating macrophage defenses.
- Using novel methodology, showed that the HIV reservoir in the brain (as detected in the CSF) in the face of ART may be in T cells.

Other contributions

- Advisor to the South African Government as part of the Technical Working Group on Vaccines.
- Led a consortium of 36 investigators in KwaZulu-Natal, South Africa (the COMMIT-KZN Team) to drive forward Covid-19 research in the province.

- Increased research visibility on international media by multiple interviews.

EDUCATION AND TRAINING

Postdoctoral Fellow, Laboratory of David Baltimore, Biology Division, The California Institute of Technology, Los Angeles, CA (1/2007 – 12/2012).

Postdoctoral Fellow, Laboratory of Uri Alon, Department of Molecular Cell Biology, The Weizmann Institute of Science, Rehovot, Israel (9/2006 – 1/2007).

Ph.D. in Systems Biology, Department of Molecular Cell Biology, The Weizmann Institute of Science, Rehovot, Israel. Advisor: Uri Alon. Completed 9/2006.

M.Sc. in Cancer Biology, Department of Molecular Cell Biology, The Weizmann Institute of Science, Rehovot, Israel. Advisor: Varda Rotter. Completed 6/2000.

B.Sc. in Zoology, University of Toronto, Toronto, Canada. Completed 6/1996.

MENTORING ACTIVITIES

- Primary supervisor for and successful graduation of 7 PhD students and 1 MSc student.
- Two of the PhD students were lead authors on Nature papers.

EDITORIAL AND OTHER EXPERIENCE

- Wellcome Trust Discovery Award Panel member (2023 – present).
- Reviewing Editor, eLife (2021 – present).
- Member, U.S.-SA Collaborative Biomedical Research Program study section ZRG1 AARR-A52 (2019) and Special Emphasis Panel/Scientific Review Group 2020/05 HCAC (2020).
- Organized the First Max Planck Workshop on HIV Reservoirs and Evolution in St. Lucia, South Africa (2019).
- Organized the First South African Workshop on SARS-CoV-2 Variants and Evolution in St. Lucia, South Africa (2022).
- Ad hoc reviewer for NEJM, Science, Nature Communications, Elife, mBio, amfAR Krim Fellowships, MBE, JID, PNAS, Wellcome Trust Henry Dale Fellowships, JAC, German Israeli Foundation grants, Nature Medicine, PLoS Comp Biol., JTM, and others.

AWARDS and HONORS

- John F. Kennedy Prize of the Weizmann Institute of Science (2006).
- European Molecular Biology Organization Fellowship (2006).
- Human Frontier Science Program Fellowship (2007).
- Human Frontier Science Program Career Development Award (2013).

PUBLICATIONS

1 Karim, F., Riou, C., Bernstein, M., Jule, Z., Lustig, G., van Graan, S., Keeton, R. S., Upton, J. L., Ganga, Y., Khan, K., Reedoy, K., Mazibuko, M., Govender, K., Thambu, K., Ngcobo, N., Venter, E., Makhado, Z., Hanekom, W., von Gottberg, A., Hoque, M., Karim, Q. A., Abdool Karim, S. S., Manickchand, N., Magula, N., Gosnell, B. I., Lessells, R. J., Moore,

P. L., Burgers, W. A., de Oliveira, T., Moosa, M. S. & **Sigal, A.** Clearance of persistent SARS-CoV-2 associates with increased neutralizing antibodies in advanced HIV disease post-ART initiation. *Nat Commun* 15, 2360 (2024). PMC10943233. 10.1038/s41467-024-46673-2

2 Lustig, G., Ganga, Y., Rodel, H. E., Tegally, H., Khairallah, A., Jackson, L., Cele, S., Khan, K., Jule, Z., Reedoy, K., Karim, F., Bernstein, M., Ndung'u, T., Moosa, M.-Y. S., Archary, D., de Oliveira, T., Lessells, R., Neher, R. A., Abdool Karim, S. S. & **Sigal, A.** SARS-CoV-2 infection in immunosuppression evolves sub-lineages which independently accumulate neutralization escape mutations. *Virus Evolution* (2023). 10.1093/ve/vead075

3 Khan, K., Lustig, G., Römer, C., Reedoy, K., Jule, Z., Karim, F., Ganga, Y., Bernstein, M., Baig, Z., Jackson, L., Mahlangu, B., Mnguni, A., Nzimande, A., Stock, N., Kekana, D., Ntozini, B., van Deventer, C., Marshall, T., Manickchand, N., Gosnell, B. I., Lessells, R. J., Karim, Q. A., Abdool Karim, S. S., Moosa, M. S., de Oliveira, T., von Gottberg, A., Wolter, N., Neher, R. A. & **Sigal, A.** Evolution and neutralization escape of the SARS-CoV-2 BA.2.86 subvariant. *Nat Commun* 14, 8078 (2023). PMC10700484. 10.1038/s41467-023-43703-3

4 Tomasicchio, M., Jaumdally, S., Wilson, L., Kotze, A., Semple, L., Meier, S., Pooran, A., Esmail, A., Pillay, K., Roberts, R., Kriel, R., Meldau, R., Oelofse, S., Mandviwala, C., Burns, J., Londt, R., Davids, M., van der Merwe, C., Roomaney, A., Kühn, L., Perumal, T., Scott, A. J., Hale, M. J., Baillie, V., Mahtab, S., Williamson, C., Joseph, R., **Sigal, A.**, Joubert, I., Piercy, J., Thomson, D., Fredericks, D. L., Miller, M. G., Nunes, M. C., Madhi, S. A. & Dheda, K. SARS-CoV-2 Viral Replication Persists in the Human Lung for Several Weeks after Symptom Onset. *Am J Respir Crit Care Med* (2024). 10.1164/rccm.202308-1438OC

5 Ng'uni, T. L., Musale, V., Nkosi, T., Mandolo, J., Mvula, M., Michelo, C., Karim, F., Moosa, M. Y. S., Khan, K., Jambo, K. C., Hanekom, W., **Sigal, A.**, Kilembe, W. & Ndhlovu, Z. M. Low pre-existing endemic human coronavirus (HCoV-NL63)-specific T cell frequencies are associated with impaired SARS-CoV-2-specific T cell responses in people living with HIV. *Frontiers in Immunology* 14 (2024). 10.3389/fimmu.2023.1291048

6 Tan, C. W., Zhu, F., Chia, W. N., Young, B. E., Yeoh, A. Y. Y., Althaus, T., Yung, C. F., Yap, W. C., Lim, B. L., Chen, M. I. C., Zhang, J., Mah, Y. Y., Voiglio, E., **Sigal, A.**, Huo, J., Xu, S., Tan, Y. J., Lam, K.-P., Lye, D. & Wang, L.-F. Distinctive serotypes of SARS-related coronaviruses defined by convalescent sera from unvaccinated individuals. *hLife* (2023). <https://doi.org/10.1016/j.hlife.2023.07.002>

7 **Sigal, A.** Boosting in the age of Omicron. *Elife* 12 (2023). PMC10110234. 10.7554/eLife.87358

- 8 Naicker, N., Rodel, H., Perumal, R., Ganga, Y., Bernstein, M., Benede, N., Abdool Karim, S., Padayatchi, N., **Sigal, A.** & Naidoo, K. Metformin Increases Cell Viability and Regulates Pro-Inflammatory Response to Mtb. *Infect Drug Resist* 16, 3629-3638 (2023). PMC10257915. 10.2147/idr.S401403
- 9 Krause, R. G. E., Moyo-Gwete, T., Richardson, S. I., Makhado, Z., Manamela, N. P., Hermanus, T., Mkhize, N. N., Keeton, R., Benede, N., Mennen, M., Skelem, S., Karim, F., Khan, K., Riou, C., Ntusi, N. A. B., Goga, A., Gray, G., Hanekom, W., Garrett, N., Bekker, L. G., Groll, A., **Sigal, A.**, Moore, P. L., Burgers, W. A. & Leslie, A. Infection pre-Ad26.COVID-2.S-vaccination primes greater class switching and reduced CXCR5 expression by SARS-CoV-2-specific memory B cells. *NPJ Vaccines* 8, 119 (2023). PMC10423246. 10.1038/s41541-023-00724-9
- 10 Kaufmann, S. H. E., **Sigal, A.**, Sawitzki, B. & Sher, A. Editorial: The Covid-19 and TB syndemic: differences and similarities. *Front Immunol* 14, 1340231 (2023). PMC10716789. 10.3389/fimmu.2023.1340231
- 11 Hysenaj, L., Little, S., Kulhanek, K., Magnen, M., Bahl, K., Gbenedio, O. M., Prinz, M., Rodriguez, L., Andersen, C., Rao, A. A., Shen, A., Lone, J. C., Lupin-Jimenez, L. C., Bonser, L. R., Serwas, N. K., Mick, E., Khalid, M. M., Taha, T. Y., Kumar, R., Li, J. Z., Ding, V. W., Matsumoto, S., Maishan, M., Sreekumar, B., Simoneau, C., Nazarenko, I., Tomlinson, M. G., Khan, K., von Gottberg, A., **Sigal, A.**, Looney, M. R., Fragiadakis, G. K., Jablons, D. M., Langelier, C. R., Matthay, M., Krummel, M., Erle, D. J., Combes, A. J., Sil, A., Ott, M., Kratz, J. R. & Roose, J. P. SARS-CoV-2 infection of airway organoids reveals conserved use of Tetraspanin-8 by Ancestral, Delta, and Omicron variants. *Stem Cell Reports* 18, 636-653 (2023). PMC9948283. 10.1016/j.stemcr.2023.01.011
- 12 Hwa, S. H., Snyman, J., Bernstein, M., Ganga, Y., Cele, S., Muema, D., Tan, C. W., Khan, K., Karim, F., Hanekom, W., Bernstein, L., Kaufmann, S. H. E., Wang, L. F., Ndung'u, T. & **Sigal, A.** Association Between Human Immunodeficiency Virus Viremia and Compromised Neutralization of Severe Acute Respiratory Syndrome Coronavirus 2 Beta Variant. *J Infect Dis* 227, 211-220 (2023). PMC9452105. 10.1093/infdis/jiac343
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- 14 Allué-Guardia, A., Torrelles, J. B. & **Sigal, A.** Tuberculosis and COVID-19 in the elderly: factors driving a higher burden of disease. *Front Immunol* 14, 1250198 (2023). PMC10569613. 10.3389/fimmu.2023.1250198

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- 17 **Sigal, A.**, Milo, R. & Jassat, W. Estimating disease severity of Omicron and Delta SARS-CoV-2 infections. *Nat Rev Immunol* 22, 267-269 (2022). PMC9002222. 10.1038/s41577-022-00720-5
- 18 **Sigal, A.** Milder disease with Omicron: is it the virus or the pre-existing immunity? *Nat Rev Immunol* 22, 69-71 (2022). 10.1038/s41577-022-00678-4
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- 21 Nkosi, T., Chasara, C., Papadopoulos, A. O., Nguni, T. L., Karim, F., Moosa, M. S., Gazy, I., Jambo, K., Hanekom, W., **Sigal, A.** & Ndhlovu, Z. M. Unsuppressed HIV infection impairs T cell responses to SARS-CoV-2 infection and abrogates T cell cross-recognition. *Elife* 11 (2022). PMC9355563. 10.7554/eLife.78374

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