Alex Sigal

Africa Health Research Institute
719 Umbilo Road
Durban, South Africa

Email: alex.sigal@ahri.org
Website: https://sigallab.net/
Twitter handle: @sigallab

Google Scholar profile:
https://scholar.google.com/citations?user=Zl7Ygk0AAAAJ&hl=en&oi=ao

Training

Institution	Degree	Completion Date	Field of study
University of Toronto	B.Sc.	06/1996	Zoology
The Weizmann Institute of Science	M.Sc.	06/2000	Cancer Biology
The Weizmann Institute of Science (Advisor: Uri Alon)	Ph.D.	09/2006	Systems Biology
The Weizmann Institute of Science (Advisor: Uri Alon)	Postdoc	01/2007	Systems Biology
California Institute of Technology (Advisor: David Baltimore)	Postdoc	12/2012	Systems Infection Biology

Personal Statement

My core research direction is understanding pathogen evolution and long term-persistence and its consequences for transmission, immune escape, and prolonged disease. I am particularly interested in the effects of immunosuppression on viral evolution.

My lab's approaches focus on cohort based human immunology merged with basic virology and immunology approaches as well as animal models. I have over 10 years of experience in running Biosafety Level 3 and 2+ facilities for SARS-CoV-2, *Mycobacterium tuberculosis* and HIV research.

Positions and Employment

2006-2007 Postdoctoral Fellow, Department of Molecular Cell Biology, Weizmann Institute of Science, Rehovot, Israel.

2007-2012 Postdoctoral Fellow, Division of Biology, California Institute of Technology, Pasadena, CA.

2012 – present Resident Faculty and Max Planck Group Leader, Africa Health Research Institute, Durban, South Africa and Max Planck Institute for Infection Biology Berlin.

2012 – present Honorary Associate Professor, University of KwaZulu-Natal.

2012 – present Associate Member, Centre for the AIDS Programme of Research in South Africa (CAPRISA).

Other Experience

2021 – Present Reviewing Editor, eLife

2019 Member, U.S.-SA Collaborative Biomedical Research Program study section ZRG1 AARR-A52

2020 Member, Special Emphasis Panel/Scientific Review Group 2020/05 HCAC

2021 – Present 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.

2021 Member, Technical Working Group on Vaccines reporting to the Ministerial Advisory Committee to the South African Government.

Awards and Honors

2006 John F. Kennedy prize for outstanding Ph.D., Weizmann Institute of Science.

2006 European Molecular Biology Organization Fellowship.

2007 Human Frontier Science Program Fellowship.

2013 Human Frontier Science Program Career Development Award.

Contribution to Science

Evolution and immune escape of SARS-CoV-2 variants: My laboratory was the first to isolate and characterize the live Beta and Omicron SARS-CoV-2 variants of concern, and the first to show using any technique that Omicron has extensive but incomplete escape of antibody immunity. We also demonstrated a possible mechanism of variant evolution that explains why Southern Africa is a hotspot for new variants.

Cele, S., Jackson, L., Khan, K., Khoury, D. S., Moyo-Gwete, T., Tegally, H., Scheepers, C., Amoako, D., Karim, F., Bernstein, M., Lustig, G., Archary, D., Smith, M., Ganga, Y., Jule, Z., Reedoy, K., Cromer, D., San, J. E., Hwa, S. H., Giandhari, J., Blackburn, J. M., Gosnell, B. I., Karim, S. S. A., Hanekom, W., Ngs, S. A., Team, C.-K., von Gottberg, A., Bhiman, J., Lessells, R. J., Moosa, M. S., Davenport, M. P., de Oliveira, T., Moore, P. L. & **Sigal, A.** Omicron extensively but incompletely escapes Pfizer BNT162b2 neutralization. Nature (first published: 23 December 2021). https://doi.org/10.1038/d41586-021-03824-5.

Cele, S., Gazy, I., Jackson, L., Hwa, S. H., Tegally, H., Lustig, G., Giandhari, J., Pillay, S., Wilkinson, E., Naidoo, Y., Karim, F., Ganga, Y., Khan, K., Bernstein, M., Balazs, A. B., Gosnell,

B. I., Hanekom, W., Moosa, M. S., Network for Genomic Surveillance in South, A., Team, C.-K., Lessells, R. J., de Oliveira, T. & **Sigal, A.** Escape of SARS-CoV-2 501Y.V2 from neutralization by convalescent plasma. Nature 593, 142-146 (2021).

Cele, S., Karim, F., Lustig, G., San, J. E., Hermanus, T., Tegally, H., Snyman, J., Moyo-Gwete, T., Wilkinson, E., Bernstein, M., Khan, K., Hwa, S. H., Tilles, S. W., Singh, L., Giandhari, J., Mthabela, N., Mazibuko, M., Ganga, Y., Gosnell, B. I., Karim, S. A., Hanekom, W., Van Voorhis, W. C., Ndunga, U. T., Team, C.-K., Lessells, R. J., Moore, P. L., Moosa, M. S., de Oliveira, T. & **Sigal, A.** SARS-CoV-2 prolonged infection during advanced HIV disease evolves extensive immune escape. Cell Host & Microbe (2022). https://doi.org/10.1016/j.chom.2022.01.005.

Khan, K., Karim, F., Cele, S., Reedoy, K., San, J. E., Lustig, G., Tegally, H., Rosenberg, Y., Bernstein, M., Jule, Z., Ganga, Y., Ngcobo, N., Mazibuko, M., Mthabela, N., Mhlane, Z., Mbatha, N., Miya, Y., Giandhari, J., Ramphal, Y., Naidoo, T., Sivro, A., Samsunder, N., Kharsany, A. B. M., Amoako, D., Bhiman, J. N., Manickchund, N., Karim, Q. A., Magula, N., Abdool Karim, S. S., Gray, G., Hanekom, W., von Gottberg, A., Milo, R., Gosnell, B. I., Lessells, R. J., Moore, P. L., de Olveira, T., Moosa, M. S. & **Sigal, A.** Omicron infection enhances Delta antibody immunity in vaccinated persons. Nature (2022).

Madhi, S. A., Baillie, V., Cutland, C. L., Voysey, M., Koen, A. L., Fairlie, L., Padayachee, S. D., Dheda, K., Barnabas, S. L., Bhorat, Q. E., Briner, C., Kwatra, G., Ahmed, K., Aley, P., Bhikha, S., Bhiman, J. N., Bhorat, A. E., du Plessis, J., Esmail, A., Groenewald, M., Horne, E., Hwa, S. H., Jose, A., Lambe, T., Laubscher, M., Malahleha, M., Masenya, M., Masilela, M., McKenzie, S., Molapo, K., Moultrie, A., Oelofse, S., Patel, F., Pillay, S., Rhead, S., Rodel, H., Rossouw, L., Taoushanis, C., Tegally, H., Thombrayil, A., van Eck, S., Wibmer, C. K., Durham, N. M., Kelly, E. J., Villafana, T. L., Gilbert, S., Pollard, A. J., de Oliveira, T., Moore, P. L., **Sigal, A.**, Izu, A. & Group, N.-S. G. W.-V. C. Efficacy of the ChAdOx1 nCoV-19 Covid-19 Vaccine against the B.1.351 Variant. N Engl J Med. 2021 May 20;384(20):1885-1898. doi: 10.1056/NEJMoa2102214. Epub 2021 Mar 16.

Cell-to-cell HIV spread and CNS compartmentalization as a reservoir in the face of ART:
I have discovered that the large number of virions transmitted by HIV cell-to-cell spread leads to reduced sensitivity to ART by a probabilistic mechanism – it increases the chance that at least one virion will escape drug action and successfully infect a cell. This mechanism can be combined with infection in compartments with low penetration of ART including the CNS.

Sigal, A., J.T. Kim, A.B. Balazs, E. Dekel, A. Mayo, R. Milo, and D. Baltimore, Cell-to-cell spread of HIV permits ongoing replication despite antiretroviral therapy. Nature, 2011. 477(7362): p. 95-8.

Lustig, G., Cele, S., Karim, F., Derache, A., Ngoepe, A., Khan, K., Gosnell, B. I., Moosa, M. S., Ntshuba, N., Marais, S., Jeena, P. M., Govender, K., Adamson, J., Kloverpris, H., Gupta, R. K., Harrichandparsad, R., Patel, V. B. & **Sigal, A**. T cell derived HIV-1 is present in the CSF in the face of suppressive antiretroviral therapy. PLoS Pathog 17, e1009871 (2021).

Aggregation of Mycobacterium tuberculosis bacilli may tip infection to active disease:
Using time-lapse microscopy, we observed that *Mycobacterium tuberculosis* (Mtb) could cause the serial killing of macrophages when it was in aggregated form.

Mahamed D, Boulle M, Ganga Y, Mc Arthur C, Skroch S, Oom L, Catinas O, Pillay K, Naicker M, Rampersad S, Mathonsi C, Hunter J, Sreejit G, Pym AS, Lustig G, **Sigal A**. Intracellular growth of Mycobacterium tuberculosis after macrophage cell death leads to serial killing of host cells. Elife. 2017;6.

List of publications:

1 Cele, S., Jackson, L., Khoury, D. S., Khan, K., Moyo-Gwete, T., Tegally, H., San, J. E., Cromer, D., Scheepers, C., Amoako, D. G., Karim, F., Bernstein, M., Lustig, G., Archary, D., Smith, M., Ganga, Y., Jule, Z., Reedoy, K., Hwa, S. H., Giandhari, J., Blackburn, J. M., Gosnell, B. I., Abdool Karim, S. S., Hanekom, W., von Gottberg, A., Bhiman, J. N., Lessells, R. J., Moosa, M. S., Davenport, M. P., de Oliveira, T., Moore, P. L. & Sigal, A. Omicron extensively but incompletely escapes Pfizer BNT162b2 neutralization. *Nature* **602**, 654-656 (2022). PMC8866126. 10.1038/s41586-021-04387-1

2 Cele, S., Gazy, I., Jackson, L., Hwa, S. H., Tegally, H., Lustig, G., Giandhari, J., Pillay, S., Wilkinson, E., Naidoo, Y., Karim, F., Ganga, Y., Khan, K., Bernstein, M., Balazs, A. B., Gosnell, B. I., Hanekom, W., Moosa, M. S., Network for Genomic Surveillance in South, A., Team, C.-K., Lessells, R. J., de Oliveira, T. & Sigal, A. Escape of SARS-CoV-2 501Y.V2 from neutralization by convalescent plasma. *Nature* **593**, 142-146 (2021). 10.1038/s41586-021-03471-w

3 Cele, S., Karim, F., Lustig, G., San, J. E., Hermanus, T., Tegally, H., Snyman, J., Moyo-Gwete, T., Wilkinson, E., Bernstein, M., Khan, K., Hwa, S. H., Tilles, S. W., Singh, L., Giandhari, J., Mthabela, N., Mazibuko, M., Ganga, Y., Gosnell, B. I., Karim, S. S. A., Hanekom, W., Van Voorhis, W. C., Ndung'u, T., Lessells, R. J., Moore, P. L., Moosa, M. S., de Oliveira, T. & Sigal, A. SARS-CoV-2 prolonged infection during advanced HIV disease evolves extensive immune escape. *Cell Host Microbe* **30**, 154-162.e155 (2022). PMC8758318. 10.1016/j.chom.2022.01.005

4 Khan, K., Karim, F., Cele, S., Reedoy, K., San, J. E., Lustig, G., Tegally, H., Rosenberg, Y., Bernstein, M., Jule, Z., Ganga, Y., Ngcobo, N., Mazibuko, M., Mthabela, N., Mhlane, Z., Mbatha, N., Miya, Y., Giandhari, J., Ramphal, Y., Naidoo, T., Sivro, A., Samsunder, N., Kharsany, A. B. M., Amoako, D., Bhiman, J. N., Manickchund, N., Karim, Q. A., Magula, N., Abdool Karim, S. S., Gray, G., Hanekom, W., von Gottberg, A., Milo, R., Gosnell, B. I., Lessells, R. J., Moore, P. L., de Olveira, T., Moosa, M. S. & Sigal, A. Omicron infection enhances Delta antibody immunity in vaccinated persons. *Nature* (2022). 10.1038/s41586-022-04830-x

5 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

6 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

7 Wells, G., Glasgow, J. N., Nargan, K., Lumamba, K., Madansein, R., Maharaj, K., Perumal, L. Y., Matthew, M., Hunter, R. L., Pacl, H., Peabody Lever, J. E., Stanford, D. D., Singh, S. P., Bajpai, P., Manne, U., Benson, P. V., Rowe, S. M., le Roux, S., Sigal, A., Tshibalanganda, M., Wells, C., du Plessis, A., Msimang, M., Naidoo, T. & Steyn, A. J. C. A high-resolution 3D atlas of the spectrum of tuberculous and COVID-19 lung lesions. *EMBO Mol Med*, e16283 (2022). 10.15252/emmm.202216283

8 Tan, C. W., Chia, W. N., Zhu, F., Young, B. E., Chantasrisawad, N., Hwa, S. H., Yeoh, A. Y., Lim, B. L., Yap, W. C., Pada, S., Tan, S. Y., Jantarabenjakul, W., Toh, L. K., Chen, S., Zhang, J., Mah, Y. Y., Chen, V. C., Chen, M. I., Wacharapluesadee, S.,

Sigal, A., Putcharoen, O., Lye, D. C. & Wang, L. F. SARS-CoV-2 Omicron variant emerged under immune selection. *Nat Microbiol* (2022). 10.1038/s41564-022-01246-1

9 Scheepers, C., Everatt, J., Amoako, D. G., Tegally, H., Wibmer, C. K., Mnguni, A., Ismail, A., Mahlangu, B., Lambson, B. E., Martin, D. P., Wilkinson, E., San, J. E., Giandhari, J., Manamela, N., Ntuli, N., Kgagudi, P., Cele, S., Richardson, S. I., Pillay, S., Mohale, T., Ramphal, U., Naidoo, Y., Khumalo, Z. T., Kwatra, G., Gray, G., Bekker, L. G., Madhi, S. A., Baillie, V., Van Voorhis, W. C., Treurnicht, F. K., Venter, M., Mlisana, K., Wolter, N., Sigal, A., Williamson, C., Hsiao, N. Y., Msomi, N., Maponga, T., Preiser, W., Makatini, Z., Lessells, R., Moore, P. L., de Oliveira, T., von Gottberg, A. & Bhiman, J. N. Emergence and phenotypic characterization of the global SARS-CoV-2 C.1.2 lineage. *Nat Commun* **13**, 1976 (2022). PMC8993834. 10.1038/s41467-022-29579-9

10 Reuschl, A. K., Mesner, D., Shivkumar, M., Whelan, M. V. X., Pallett, L. J., Guerra-Assunção, J. A., Madansein, R., Dullabh, K. J., Sigal, A., Thornhill, J. P., Herrera, C., Fidler, S., Noursadeghi, M., Maini, M. K. & Jolly, C. HIV-1 Vpr drives a tissue residency-like phenotype during selective infection of resting memory T cells. *Cell Rep* **39**, 110650 (2022). 10.1016/j.celrep.2022.110650

11 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

12 Meng, B., Abdullahi, A., Ferreira, I., Goonawardane, N., Saito, A., Kimura, I., Yamasoba, D., Gerber, P. P., Fatihi, S., Rathore, S., Zepeda, S. K., Papa, G., Kemp, S. A., Ikeda, T., Toyoda, M., Tan, T. S., Kuramochi, J., Mitsunaga, S., Ueno, T., Shirakawa, K., Takaori-Kondo, A., Brevini, T., Mallery, D. L., Charles, O. J., Bowen, J. E., Joshi, A., Walls, A. C., Jackson, L., Martin, D., Smith, K. G. C., Bradley, J., Briggs, J. A. G., Choi, J., Madissoon, E., Meyer, K. B., Mlcochova, P., Ceron-Gutierrez, L., Doffinger, R., Teichmann, S. A., Fisher, A. J., Pizzuto, M. S., de Marco, A., Corti, D., Hosmillo, M., Lee, J. H., James, L. C., Thukral, L., Veesler, D., Sigal, A., Sampaziotis, F., Goodfellow, I. G., Matheson, N. J., Sato, K. & Gupta, R. K. Altered TMPRSS2 usage by SARS-CoV-2 Omicron impacts infectivity and fusogenicity. *Nature* **603**, 706-714 (2022). PMC8942856. 10.1038/s41586-022-04474-x

13 Martin, D. P., Lytras, S., Lucaci, A. G., Maier, W., Grüning, B., Shank, S. D., Weaver, S., MacLean, O. A., Orton, R. J., Lemey, P., Boni, M. F., Tegally, H., Harkins, G. W., Scheepers, C., Bhiman, J. N., Everatt, J., Amoako, D. G., San, J. E., Giandhari, J., Sigal, A., Williamson, C., Hsiao, N. Y., von Gottberg, A., De Klerk, A., Shafer, R. W., Robertson, D. L., Wilkinson, R. J., Sewell, B. T., Lessells, R., Nekrutenko, A., Greaney, A. J., Starr, T. N., Bloom, J. D., Murrell, B., Wilkinson, E., Gupta, R. K., de Oliveira, T. & Kosakovsky Pond, S. L. Selection Analysis Identifies Clusters of Unusual Mutational Changes in Omicron Lineage BA.1 That Likely Impact Spike Function. *Mol Biol Evol* **39** (2022). PMC9037384. 10.1093/molbev/msac061

14 Krause, R., Snyman, J., Shi-Hsia, H., Muema, D., Karim, F., Ganga, Y., Ngoepe, A., Zungu, Y., Gazy, I., Bernstein, M., Khan, K., Mazibuko, M., Mthabela, N., Ramjit, D., Limbo, O., Jardine, J., Sok, D., Wilson, I. A., Hanekom, W., Sigal, A., Kløverpris, H., Ndung'u, T. & Leslie, A. HIV skews the SARS-CoV-2 B cell response toward an extrafollicular maturation pathway. *Elife* **11** (2022). 10.7554/eLife.79924

15 Khan, K., Karim, F., Ganga, Y., Bernstein, M., Jule, Z., Reedoy, K., Cele, S., Lustig, G., Amoako, D., Wolter, N., Samsunder, N., Sivro, A., San, J. E., Giandhari, J., Tegally, H., Pillay, S., Naidoo, Y., Mazibuko, M., Miya, Y., Ngcobo, N., Manickchund, N., Magula, N., Karim, Q. A., von Gottberg, A., Abdool Karim, S. S., Hanekom, W., Gosnell, B. I., Lessells, R. J., de Oliveira, T., Moosa, M. S. & Sigal, A. Omicron BA.4/BA.5 escape neutralizing immunity elicited by BA.1 infection. *Nat Commun* **13**, 4686 (2022). PMC9364294. 10.1038/s41467-022-32396-9

16 Keeton, R., Tincho, M. B., Ngomti, A., Baguma, R., Benede, N., Suzuki, A., Khan, K., Cele, S., Bernstein, M., Karim, F., Madzorera, S. V., Moyo-Gwete, T., Mennen, M., Skelem, S., Adriaanse, M., Mutithu, D., Aremu, O., Stek, C., du Bruyn, E., Van Der Mescht, M. A., de Beer, Z., de Villiers, T. R., Bodenstein, A., van den Berg, G., Mendes, A., Strydom, A., Venter, M., Giandhari, J., Naidoo, Y., Pillay, S., Tegally, H., Grifoni, A., Weiskopf, D., Sette, A., Wilkinson, R. J., de Oliveira, T., Bekker, L. G., Gray, G., Ueckermann, V., Rossouw, T., Boswell, M. T., Bhiman, J. N., Moore, P. L., Sigal, A., Ntusi, N. A. B., Burgers, W. A. & Riou, C. T cell responses to SARS-CoV-2 spike cross-recognize Omicron. *Nature* **603**, 488-492 (2022). PMC8930768. 10.1038/s41586-022-04460-3

17 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. HIV viremia is associated with compromised SARS-CoV-2 Beta variant neutralization. *J Infect Dis* (2022). PMC9452105. 10.1093/infdis/jiac343

18 Greaney, A. J., Starr, T. N., Eguia, R. T., Loes, A. N., Khan, K., Karim, F., Cele, S., Bowen, J. E., Logue, J. K., Corti, D., Veesler, D., Chu, H. Y., Sigal, A. & Bloom, J. D. A SARS-CoV-2 variant elicits an antibody response with a shifted immunodominance hierarchy. *PLoS Pathog* **18**, e1010248 (2022). PMC8856557. 10.1371/journal.ppat.1010248

19 Greaney, A. J., Eguia, R. T., Starr, T. N., Khan, K., Franko, N., Logue, J. K., Lord, S. M., Speake, C., Chu, H. Y., Sigal, A. & Bloom, J. D. The SARS-CoV-2 Delta variant induces an antibody response largely focused on class 1 and 2 antibody epitopes. *PLoS Pathog* **18**, e1010592 (2022). PMC9275729. 10.1371/journal.ppat.1010592

20 Cele, S., Bernstein, M., Karim, F., Khan, K., Ganga, Y., Jule, Z., Reedoy, K., Lustig, G., Samsunder, N., Mazibuko, M., Hwa, S.-H., Manickchund, N., Gottberg, A. v., Magula, N., Lessells, R. J., de Oliveira, T., Abdool Karim, S. S., Hanekom, W., Gosnell, B. I., Moosa, M.-Y. S. & Sigal, A. Beta infection combined with Pfizer BNT162b2 vaccination leads to broadened neutralizing immunity against Omicron. *medRxiv*, 2022.2004.2015.22273711 (2022). 10.1101/2022.04.15.22273711

21 Tegally, H., Wilkinson, E., Lessells, R. J., Giandhari, J., Pillay, S., Msomi, N., Mlisana, K., Bhiman, J. N., von Gottberg, A., Walaza, S., Fonseca, V., Allam, M., Ismail, A., Glass, A. J., Engelbrecht, S., Van Zyl, G., Preiser, W., Williamson, C., Petruccione, F., Sigal, A., Gazy, I., Hardie, D., Hsiao, N. Y., Martin, D., York, D., Goedhals, D., San, E. J., Giovanetti, M., Lourenco, J., Alcantara, L. C. J. & de Oliveira, T. Sixteen novel lineages of SARS-CoV-2 in South Africa. *Nat Med* **27**, 440-446 (2021). 10.1038/s41591-021-01255-3

22 Tegally, H., Wilkinson, E., Giovanetti, M., Iranzadeh, A., Fonseca, V., Giandhari, J., Doolabh, D., Pillay, S., San, E. J., Msomi, N., Mlisana, K., von Gottberg, A., Walaza, S., Allam, M., Ismail, A., Mohale, T., Glass, A. J., Engelbrecht, S., Van Zyl, G., Preiser, W., Petruccione, F., Sigal, A., Hardie, D., Marais, G., Hsiao, N. Y., Korsman, S., Davies, M. A., Tyers, L., Mudau, I., York, D., Maslo, C., Goedhals, D., Abrahams, S.,

Laguda-Akingba, O., Alisoltani-Dehkordi, A., Godzik, A., Wibmer, C. K., Sewell, B. T., Lourenço, J., Alcantara, L. C. J., Kosakovsky Pond, S. L., Weaver, S., Martin, D., Lessells, R. J., Bhiman, J. N., Williamson, C. & de Oliveira, T. Detection of a SARS-CoV-2 variant of concern in South Africa. *Nature* **592**, 438-443 (2021). 10.1038/s41586-021-03402-9

23 Snyman, J., Hwa, S. H., Krause, R., Muema, D., Reddy, T., Ganga, Y., Karim, F., Leslie, A., Sigal, A. & Ndung'u, T. Similar antibody responses against SARS-CoV-2 in HIV uninfected and infected individuals on antiretroviral therapy during the first South African infection wave. *Clin Infect Dis* (2021). PMC8522359. 10.1093/cid/ciab758

24 Skelly, D. T., Harding, A. C., Gilbert-Jaramillo, J., Knight, M. L., Longet, S., Brown, A., Adele, S., Adland, E., Brown, H., Medawar Laboratory, T., Tipton, T., Stafford, L., Mentzer, A. J., Johnson, S. A., Amini, A., Group, O. C., Tan, T. K., Schimanski, L., Huang, K. A., Rijal, P., Group, P. S., Group, C. M. P.-C., Frater, J., Goulder, P., Conlon, C. P., Jeffery, K., Dold, C., Pollard, A. J., Sigal, A., de Oliveira, T., Townsend, A. R., Klenerman, P., Dunachie, S. J., Barnes, E., Carroll, M. W. & James, W. S. Two doses of SARS-CoV-2 vaccination induce robust immune responses to emerging SARS-CoV-2 variants of concern. *Nat Commun* **12**, 5061 (2021). PMC8371089. 10.1038/s41467-021-25167-5

25 Rodel, H. E., Ferreira, I., Ziegler, C. G. K., Ganga, Y., Bernstein, M., Hwa, S. H., Nargan, K., Lustig, G., Kaplan, G., Noursadeghi, M., Shalek, A. K., Steyn, A. J. C. & Sigal, A. Aggregated Mycobacterium tuberculosis Enhances the Inflammatory Response. *Front Microbiol* **12**, 757134 (2021). PMC8674758. 10.3389/fmicb.2021.757134

26 Madhi, S. A., Baillie, V., Cutland, C. L., Voysey, M., Koen, A. L., Fairlie, L., Padayachee, S. D., Dheda, K., Barnabas, S. L., Bhorat, Q. E., Briner, C., Kwatra, G., Ahmed, K., Aley, P., Bhikha, S., Bhiman, J. N., Bhorat, A. E., du Plessis, J., Esmail, A., Groenewald, M., Horne, E., Hwa, S. H., Jose, A., Lambe, T., Laubscher, M., Malahleha, M., Masenya, M., Masilela, M., McKenzie, S., Molapo, K., Moultrie, A., Oelofse, S., Patel, F., Pillay, S., Rhead, S., Rodel, H., Rossouw, L., Taoushanis, C., Tegally, H., Thombrayil, A., van Eck, S., Wibmer, C. K., Durham, N. M., Kelly, E. J., Villafana, T. L., Gilbert, S., Pollard, A. J., de Oliveira, T., Moore, P. L., Sigal, A. & Izu, A. Efficacy of the ChAdOx1 nCoV-19 Covid-19 Vaccine against the B.1.351 Variant. *N Engl J Med* **384**, 1885-1898 (2021). PMC7993410. 10.1056/NEJMoa2102214

27 Lustig, G., Cele, S., Karim, F., Derache, A., Ngoepe, A., Khan, K., Gosnell, B. I., Moosa, M. S., Ntshuba, N., Marais, S., Jeena, P. M., Govender, K., Adamson, J., Kloverpris, H., Gupta, R. K., Harrichandparsad, R., Patel, V. B. & Sigal, A. T cell derived HIV-1 is present in the CSF in the face of suppressive antiretroviral therapy. *PLoS Pathog* **17**, e1009871 (2021). PMC8509856 10.1371/journal.ppat.1009871

28 Kolloli, A., Kumar, R., Singh, P., Narang, A., Kaplan, G., Sigal, A. & Subbian, S. Aggregation state of Mycobacterium tuberculosis impacts host immunity and augments pulmonary disease pathology. *Commun Biol* **4**, 1256 (2021). PMC8566596. 10.1038/s42003-021-02769-9

29 Khan, K., Lustig, G., Bernstein, M., Archary, D., Cele, S., Karim, F., Smith, M., Ganga, Y., Jule, Z., Reedoy, K., Miya, Y., Mthabela, N., Magula, N. P., Lessells, R., de Oliveira, T., Gosnell, B. I., Karim, S. A., Garrett, N., Hanekom, W., Gail-Bekker, L., Gray, G., Blackburn, J. M., Moosa, M. S. & Sigal, A. Immunogenicity of SARS-CoV-2 infection and Ad26.CoV2.S vaccination in people living with HIV. *Clin Infect Dis* (2021). PMC8689810. 10.1093/cid/ciab1008

30 Karim, F., Moosa, M., Gosnell, B., Cele, S., Giandhari, J., Pillay, S., Tegally, H., Wilkinson, E., San, J., Msomi, N., Mlisana, K., Khan, K., Bernstein, M., Manickchund, N., Singh, L., Ramphal, U., Hanekom, W., Lessells, R., Sigal, A. & de Oliveira, T. Persistent SARS-CoV-2 infection and intra-host evolution in association with advanced HIV infection. *medRxiv*, 2021.2006.2003.21258228 (2021). 10.1101/2021.06.03.21258228

31 Karim, F., Gazy, I., Cele, S., Zungu, Y., Krause, R., Bernstein, M., Khan, K., Ganga, Y., Rodel, H., Mthabela, N., Mazibuko, M., Muema, D., Ramjit, D., Ndung'u, T., Hanekom, W., Gosnell, B., Lessells, R. J., Wong, E. B., de Oliveira, T., Moosa, M. S., Lustig, G., Leslie, A., Kløverpris, H. & Sigal, A. HIV status alters disease severity and immune cell responses in Beta variant SARS-CoV-2 infection wave. *Elife* **10** (2021). PMC8676326. 10.7554/eLife.67397

32 Garcia-Beltran, W. F., Lam, E. C., St Denis, K., Nitido, A. D., Garcia, Z. H., Hauser, B. M., Feldman, J., Pavlovic, M. N., Gregory, D. J., Poznansky, M. C., Sigal, A., Schmidt, A. G., Iafrate, A. J., Naranbhai, V. & Balazs, A. B. Multiple SARS-CoV-2 variants escape neutralization by vaccine-induced humoral immunity. *Cell* **184**, 2523 (2021). PMC8082941. 10.1016/j.cell.2021.04.006

33 Faulkner, N., Ng, K. W., Wu, M. Y., Harvey, R., Margaritis, M., Paraskevopoulou, S., Houlihan, C., Hussain, S., Greco, M., Bolland, W., Warchal, S., Heaney, J., Rickman, H., Spyer, M., Frampton, D., Byott, M., de Oliveira, T., Sigal, A., Kjaer, S., Swanton, C., Gandhi, S., Beale, R., Gamblin, S. J., McCauley, J. W., Daniels, R. S., Howell, M., Bauer, D., Nastouli, E. & Kassiotis, G. Reduced antibody cross-reactivity following infection with B.1.1.7 than with parental SARS-CoV-2 strains. *Elife* **10** (2021). PMC8352583. 10.7554/eLife.69317

34 Cromarty, R., Sigal, A., Liebenberg, L. J., McKinnon, L. R., Abdool Karim, S. S., Passmore, J. S. & Archary, D. Betamethasone induces potent immunosuppression and reduces HIV infection in a PBMC in vitro model. *J Investig Med* **69**, 28-40 (2021). PMC7803916. 10.1136/jim-2020-001424

35 Moyano, A., Lustig, G., Rodel, H. E., Antal, T. & Sigal, A. Interference with HIV infection of the first cell is essential for viral clearance at sub-optimal levels of drug inhibition. *PLoS Comput Biol* **16**, e1007482 (2020). PMC7039526. 10.1371/journal.pcbi.1007482

36 Kim, J. T., Chang, E., Sigal, A. & Baltimore, D. Dendritic cells efficiently transmit HIV to T Cells in a tenofovir and raltegravir insensitive manner. *PloS one* **13**, e0189945 (2018).

37 Jackson, L., Hunter, J., Cele, S., Ferreira, I. M., Young, A. C., Karim, F., Madansein, R., Dullabh, K. J., Chen, C. Y., Buckels, N. J., Ganga, Y., Khan, K., Boulle, M., Lustig, G., Neher, R. A. & Sigal, A. Incomplete inhibition of HIV infection results in more HIV infected lymph node cells by reducing cell death. *Elife* **7** (2018). PMC5896883. 10.7554/eLife.30134

38 Barichievy, S., Naidoo, J., Boulle, M., Scholefield, J., Parihar, S. P., Coussens, A. K., Brombacher, F., Sigal, A. & Mhlanga, M. M. Viral Apoptosis Evasion via the MAPK Pathway by Use of a Host Long Noncoding RNA. *Front Cell Infect Microbiol* **8**, 263 (2018). PMC6086015. 10.3389/fcimb.2018.00263

39 Mahamed, D., Boulle, M., Ganga, Y., Mc Arthur, C., Skroch, S., Oom, L., Catinas, O., Pillay, K., Naicker, M., Rampersad, S., Mathonsi, C., Hunter, J., Sreejit, G., Pym, A.

S., Lustig, G. & Sigal, A. Intracellular growth of Mycobacterium tuberculosis after macrophage cell death leads to serial killing of host cells. *Elife* **6** (2017). 10.7554/eLife.22028

40 Boulle, M., Muller, T. G., Dahling, S., Ganga, Y., Jackson, L., Mahamed, D., Oom, L., Lustig, G., Neher, R. A. & Sigal, A. HIV Cell-to-Cell Spread Results in Earlier Onset of Viral Gene Expression by Multiple Infections per Cell. *PLoS Pathog* **12**, e1005964 (2016). 10.1371/journal.ppat.1005964

41 Farkash-Amar, S., Zimmer, A., Eden, E., Cohen, A., Geva-Zatorsky, N., Cohen, L., Milo, R., Sigal, A., Danon, T. & Alon, U. Noise genetics: inferring protein function by correlating phenotype with protein levels and localization in individual human cells. *PLoS Genet* **10**, e1004176 (2014). PMC3945223. 10.1371/journal.pgen.1004176

42 Costiniuk, C. T., Sigal, A., Jenabian, M. A., Nijs, P. & Wilson, D. Short communication: Lower baseline CD4 count is associated with a greater propensity toward virological failure in a cohort of South African HIV patients. *AIDS Res Hum Retroviruses* **30**, 531-534 (2014). 10.1089/AID.2014.0011

43 Sigal, A. & Baltimore, D. As good as it gets? The problem of HIV persistence despite antiretroviral drugs. *Cell Host Microbe* **12**, 132-138 (2012). 10.1016/j.chom.2012.07.005

44 Puliafito, A., Hufnagel, L., Neveu, P., Streichan, S., Sigal, A., Fygenson, D. K. & Shraiman, B. I. Collective and single cell behavior in epithelial contact inhibition. *Proc Natl Acad Sci U S A* **109**, 739-744 (2012). PMC3271933. 10.1073/pnas.1007809109

45 Farkash-Amar, S., Eden, E., Cohen, A., Geva-Zatorsky, N., Cohen, L., Milo, R., Sigal, A., Danon, T. & Alon, U. Dynamic proteomics of human protein level and localization across the cell cycle. *PLoS One* **7**, e48722 (2012). PMC3492413. 10.1371/journal.pone.0048722

46 Sigal, A., Kim, J. T., Balazs, A. B., Dekel, E., Mayo, A., Milo, R. & Baltimore, D. Cell-to-cell spread of HIV permits ongoing replication despite antiretroviral therapy. *Nature* **477**, 95-98 (2011). 10.1038/nature10347

47 Frenkel-Morgenstern, M., Cohen, A. A., Geva-Zatorsky, N., Eden, E., Prilusky, J., Issaeva, I., Sigal, A., Cohen-Saidon, C., Liron, Y., Cohen, L., Danon, T., Perzov, N. & Alon, U. Dynamic Proteomics: a database for dynamics and localizations of endogenous fluorescently-tagged proteins in living human cells. *Nucleic Acids Res* **38**, D508-512 (2010). 2808965. 10.1093/nar/gkp808

48 Cohen-Saidon, C., Cohen, A. A., Sigal, A., Liron, Y. & Alon, U. Dynamics and variability of ERK2 response to EGF in individual living cells. *Mol Cell* **36**, 885-893 (2009). 10.1016/j.molcel.2009.11.025

49 Cohen, A. A., Kalisky, T., Mayo, A., Geva-Zatorsky, N., Danon, T., Issaeva, I., Kopito, R. B., Perzov, N., Milo, R., Sigal, A. & Alon, U. Protein dynamics in individual human cells: experiment and theory. *PLoS One* **4**, e4901 (2009). PMC2668709. 10.1371/journal.pone.0004901

50 Cohen, A. A., Geva-Zatorsky, N., Eden, E., Frenkel-Morgenstern, M., Issaeva, I., Sigal, A., Milo, R., Cohen-Saidon, C., Liron, Y., Kam, Z., Cohen, L., Danon, T., Perzov, N. & Alon, U. Dynamic proteomics of individual cancer cells in response to a drug. *Science* **322**, 1511-1516 (2008). 10.1126/science.1160165

51 Sigal, A., Danon, T., Cohen, A., Milo, R., Geva-Zatorsky, N., Lustig, G., Liron, Y., Alon, U. & Perzov, N. Generation of a fluorescently labeled endogenous protein library in living human cells. *Nat Protoc* **2**, 1515-1527 (2007). 10.1038/nprot.2007.197

52 Lavelle, C. & Sigal, A. Systems biology meets chromatin function: a report on the Fourth Elmau Conference on Nuclear Organization. *Chromosome Res* **15**, 247-256 (2007). 10.1007/s10577-006-1118-6

53 Sigal, A., Milo, R., Cohen, A., Geva-Zatorsky, N., Klein, Y., Liron, Y., Rosenfeld, N., Danon, T., Perzov, N. & Alon, U. Variability and memory of protein levels in human cells. *Nature* **444**, 643-646 (2006). 10.1038/nature05316

54 Sigal, A., Milo, R., Cohen, A., Geva-Zatorsky, N., Klein, Y., Alaluf, I., Swerdlin, N., Perzov, N., Danon, T., Liron, Y., Raveh, T., Carpenter, A. E., Lahav, G. & Alon, U. Dynamic proteomics in individual human cells uncovers widespread cell-cycle dependence of nuclear proteins. *Nat Methods* **3**, 525-531 (2006). 10.1038/nmeth892

55 Geva-Zatorsky, N., Rosenfeld, N., Itzkovitz, S., Milo, R., Sigal, A., Dekel, E., Yarnitzky, T., Liron, Y., Polak, P., Lahav, G. & Alon, U. Oscillations and variability in the p53 system. *Mol Syst Biol* **2**, 2006 0033 (2006). PMC1681500. 10.1038/msb4100068

56 Lahav, G., Rosenfeld, N., Sigal, A., Geva-Zatorsky, N., Levine, A. J., Elowitz, M. B. & Alon, U. Dynamics of the p53-Mdm2 feedback loop in individual cells. *Nat Genet* **36**, 147-150 (2004). 10.1038/ng1293

57 Sigal, A., Matas, D., Almog, N., Goldfinger, N. & Rotter, V. The C-terminus of mutant p53 is necessary for its ability to interfere with growth arrest or apoptosis. *Oncogene* **20**, 4891-4898 (2001). 10.1038/sj.onc.1204724

58 Seluanov, A., Gorbunova, V., Falcovitz, A., Sigal, A., Milyavsky, M., Zurer, I., Shohat, G., Goldfinger, N. & Rotter, V. Change of the death pathway in senescent human fibroblasts in response to DNA damage is caused by an inability to stabilize p53. *Mol Cell Biol* **21**, 1552-1564 (2001). 86701. 10.1128/MCB.21.5.1552-1564.2001

59 Matas, D., Sigal, A., Stambolsky, P., Milyavsky, M., Weisz, L., Schwartz, D., Goldfinger, N. & Rotter, V. Integrity of the N-terminal transcription domain of p53 is required for mutant p53 interference with drug-induced apoptosis. *EMBO J* **20**, 4163-4172 (2001). 149170. 10.1093/emboj/20.15.4163

60 Sigal, A. & Rotter, V. Oncogenic mutations of the p53 tumor suppressor: the demons of the guardian of the genome. *Cancer Res* **60**, 6788-6793 (2000).

61 Sigal, A., Bleijs, D. A., Grabovsky, V., van Vliet, S. J., Dwir, O., Figdor, C. G., van Kooyk, Y. & Alon, R. The LFA-1 integrin supports rolling adhesions on ICAM-1 under physiological shear flow in a permissive cellular environment. *J Immunol* **165**, 442-452 (2000). ji_v165n1p442

Book Chapter

Sigal, A. & Rotter, V. in The p53 Tumor Suppressor Pathway and Cancer Vol. 2 Protein Reviews (ed Gerard P. Zambetti) Ch. 9, 199-223 (Springer, 2005).

Patents

1) WO 2009/093242 A2. CELL POPULATIONS FOR POLYPEPTIDE ANALYSIS AND USES OF SAME.
2) U.S. Ser. No. 62/573,049. MYCOBACTERIUM TUBERCULOSIS HOST-PATHOGEN INTERACTION.
3) U.S. Ser. No. 62/573,025. MARKERS OF ACTIVE HIV RESERVOIR.

Recent invited talks (2021-2022)

Milder disease with Omicron: Is it the virus, pre-existing immunity, and will our immunity protect us from the next variant? First South African Workshop on SARS-COV-2 Variants and Evolution 31 October – 3November 2022, St. Lucia, South Africa.

Milder disease with Omicron: Is it the virus, pre-existing immunity, and will our immunity protect us from the next variant? Grand Challenges Annual Meeting 23-26 October 2022, Brussels, Belgium.

Milder disease with Omicron: Is it the virus, pre-existing immunity, and will our immunity protect us from the next variant? Second plenary, South African Immunological Society Annual Conference, 2-4 October, Muldersdrift, South Africa.

Milder disease with Omicron: Is it the virus, pre-existing immunity, and will our immunity protect us from the next variant? Weizmann Institute of Science Immunology and Regenerative Biology Colloquium Invited Speaker, 10 July 2022, Rehovot, Israel.

Evolution of SARS-CoV-2 in South Africa and in PLWH. United States – Japan Cooperative Medical Sciences Program. 8-10 March 2022 (virtual).

Milder disease with Omicron: Is it the virus, pre-existing immunity, and will our immunity protect us from the next variant? 9th Winter qBio, 14-18 February 2022, Oahu, Hawaii.

Session Chair with two students presenting: Association of HIV Infection with Worse COVID-19 Outcomes and Intra-Host Evolution of SARS-CoV-2 (Farina Karim, Sigal Lab); Beta and Delta Variants are Serologically Distinct with Prolonged SARS-CoV-2 Infection Evolving a Beta-Like Phenotype (Sandile Cele, Sigal Lab). Collaboration for AIDS Vaccine Discovery (CAVD), 15-17 November 2021 (virtual).

Divergence of Delta and Beta variants and SARS-CoV-2 evolved in prolonged infection into distinct serological phenotypes (keynote). 8th European Seminar in Virology (EuSeV), Innate and adaptive immunity to SARS-CoV2 and other viruses, 15th-17th October 2021, Bertinoro, Italy.

Moving Target: Interactions of HIV co-infection and SARS-CoV-2 variants of concern. 11th International AIDS Society Conference (IAS 2021), 18-21 July 2021 (virtual).

Impact of HIV co-infection on COVID-19 outcomes. Neurologic and Psychiatric Effects of SARS-CoV-2 Meeting, 14-15 July 2021 (virtual).

Moving Target: Interactions of HIV co-infection and SARS-CoV-2 variants of concern. 31st European Congress of Clinical Microbiology & Infectious Diseases 9 – 12 July 2021 (virtual).

Evolution and persistence of SARS-CoV-2 in the face of immune pressure. Human Cell Atlas General Meeting, 30 June 2021 (virtual).

Conferences organized

Max Planck Workshop on HIV Reservoirs and Evolution
January 20-23, 2019, St. Lucia, South Africa.
https://www.hivreservoirsandevolution.com/

First South African Workshop on SARS-COV-2 Variants and Evolution
October 31 – November 3, 2022, St. Lucia, South Africa.
https://sarscov2variants.net/

Advising and mentoring

Postdoctoral

Dr. Deeqa Mahamed (Postdoctoral Fellow, Sigal Lab). Current: Research Associate, The Hospital for Sick Children, Toronto, Canada.

Dr. Laurelle Jackson (PhD and Postdoctoral Fellow, Sigal Lab). Current: Research Associate, College of Medicine and Public Health, Flinders University, Adelaide, Australia.

Doctoral

Dr. Sandile Cele (PhD Sigal Lab). Current: Laboratory Supervisor, Sigal Lab, AHRI.

Dr. Shi-Hsia Hwa (PhD Sigal Lab). Current: Postdoctoral Fellow, Laboratory of Immunogenetics, NIAID, NIH, Bethesda, USA.

Dr. Jessica Hunter (PhD Sigal Lab). Current: Researcher at Theolytics Ltd, Oxford, UK.

M.Sc. and MD Thesis

Dr. Isabella Ferreira (MSc Sigal Lab). Current: PhD Cambridge University, Cambridge, UK (completed, currently Postdoc at Cornell University).

Dr. Mikael Boulle (MD Thesis Sigal Lab). Current: Postdoctoral Fellow, Institut Pasteur, Paris, France.

Current Candidates

Farina Karim (PhD candidate).

Khadija Khan (PhD candidate).

Hylton Rodel (PhD candidate).

Research Support

2022-2025	Wellcome Trust	Adaptive responses to SARS-CoV-2 variants in the context of hybrid immunity and immune impairment	$3,890,304	Principal Investigator

2020-2025	BMGF	COVID-19 Mechanisms and Multi-omics in KwaZulu-Natal	$4,027,703	Principal Investigator
2022-2023	NIH	Evolution of innate immunity and antibody neutralization escape mutations in prolonged SARS-CoV-2 infection in people with advanced HIV (part of United World Antiviral Research Network (UWARN) collaboration)	$216,156	Co-Investigator
2022-2023	BMGF	BaSiS Trial Phase 2 clinical study extension	$471,512	Co-Investigator
2022-2023	South African Medical Research Council	Phase II randomised open label trial of full and half dose J&J Ad26.COV2.S and Pfizer BNT162b2 booster vaccinations after receiving the J&J Ad26.COV2.S prime vaccine through the SISONKE phase IIIB implementation study (BaSiS Trial)	ZAR 1,496,796 ($91,921)	Co-Investigator
2022-2025	South African Medical Research Council	Immunogenicity studies for mRNA vaccine candidate development	ZAR 4,659,787 ($286,166)	Co-Investigator
2021-2023	South African Medical Research Council	Neutralization escape from antibodies elicited by vaccines	ZAR 2,525,313 ($155,084)	Principal Investigator
2012-2020	Max Planck Society	Group Leader Award: The purpose of this award is to set up a Systems Infection Biology Group at K-RITH/AHRI investigating persistent infection of TB and HIV in the face of the immune response and therapy.	€1,924,192	Principal Investigator
2018-2023	NIH-NIAID	Identification of the HIV Reservoir in Lymph Nodes Using Single Cell RNA-Seq	$721,310	Principal Investigator
2014-2021	HHMI	IgG penetration into the TB granuloma	$72,000	Principal Investigator

2018-2021	amfAR	HIV persistence in lymph nodes in the face of ART in TB-infected individuals.	$50,000	Principal Investigator
2020-2021	AHRI	COVID-19 Infection Dynamics in PLWH vs HIV- Individuals	R 998,832 ($61,605)	Principal Investigator
2014-2019	BMGF	Quantitative assessment of the tipping point in Mycobacterium tuberculosis transmission and infection	$2,214,804	Principal Investigator
2015-2019	EU commission	Role of TB antibodies (part of TBVAC2020 consortium)	€167,227	Principal Investigator
2017-2019	HHMI	Identification and Targeting HIV in the CNS Reservoir	$60,000	Principal Investigator
2013-2017	HFSP	Using probability theory to understand the formation of a reservoir of drug insensitive infection	$300,000	Principal Investigator
2014-2017	NIH-NIMH-NIAID	Ongoing HIV replication as a CNS persistence mechanism in the face of antiretroviral therapy	$297,000	Principal Investigator
2013-2014	HHMI	Screening for new T-cell receptor and antibody genes reactive to Mycobacterium tuberculosis.	$75,000	Principal Investigator