

Spatiotemporal regulation of humoral immunity

Curriculum Vitae

Personal Data

Tal I Arnon, PhD
 The University of Oxford,
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Education

1999 B.A. in Life Sciences, Hebrew University of Jerusalem, Givat-Ram, Israel. grade: distinction
 2006 Ph.D. in Microbiology and Immunology, Hebrew University of Jerusalem, Hadassah Medical School, Israel, summa cum laude

Positions and Employment

2022-present	The Kennedy Institute, Oxford, UK	Tenured associate Professor
2020-2022	The Kennedy Institute, Oxford, UK	Associate Professor
2014-2020	The Kennedy Institute, Oxford, UK	Senior research fellow
2008-2014	UCSF, Prof. Jason G. Cyster's lab, USA	Postdoctoral fellow
2006-2008	Caltech, Prof. Pamela Bjorkman's lab, USA	Postdoctoral fellow

Selected Awards and fellowships

2021	Wellcome Trust Investigator Award	Investigator Award
2015	Wellcome Trust Investigator Award	Investigator Award
2014	The Kennedy Trust of Rheumatology	Senior Research Fellowship
2006	Jane Coffin Childs Fund	Postdoctoral Fellowship

Current research Funding

- 2023-29 Wellcome Trust Investigator Award 'Spatiotemporal basis of adaptive immunity in the spleen' (PI) £1,527,379. **This funding can be transferred to other countries / institutions.**
- 2022-26 MRC project grant, Orchestrating resident memory B cell responses in the lung during secondary infection with influenza virus (PI) £823,088.
- 2021-23 Bristol-Myers Squibb. 'Testing noncanonical regulators of T cell trafficking to enhance tumor infiltration' (Co-PI, together with Prof. Audrey Gerald) \$500,000.
- 2021-25, Kennedy Trust for Rheumatology Research Cell Dynamics Strategy (co-I), £175,629.
- 2020-23 John Fell Fund. "Regional humoral immunity in the lung; exploring the roles of resident memory B cells in protection against influenza virus" (PI) £45,020.
- 2016, Wellcome Multiuser Equipment Grant (co-I) In vivo microscopy system to probe microbiome link to inflammation. £284,000 plus £284,000 from Kennedy Trust matching grant.

Invited speaker talks in National and International conferences (in person)

2019 Trinity meeting 'From lab to Clinic', Oxford
 2019 Future of Immunology and Berlin' Symposium; Germany
 2021 Karolinska Institute Immunology retreat; Sweden
 2021 British Society of Immunology (BSI) Congress; Scotland

- 2022 Chemotactic Cytokine Gordon Research Conference; Switzerland
- 2022 Scotland-wide meeting, Invited speaker; Scotland
- 2022 Berlin-Oxford summer School; Germany
- 2023 Imaging the Immune System; Switzerland
- 2023 Imaging Cell Dynamic; Portugal
- 2024 Pathogen Immunity and Signalling, EMBO meeting; Italy
- 2024 Swiss Allergology and Immunology meeting (SSAI); Switzerland

Invited speaker in International seminars

- 2018 Kanton Hospital St. Gallen (KSSG), external seminar series; Switzerland
- 2019 The CIML, external seminar series; France
- 2022 Heidelberg University, external seminar series; Germany
- 2022 Wurzburg University, external seminar series; Germany

Invited speaker in national seminars

- 2015 Imperial College, external seminar series; London
- 2016 Babraham Institute, external seminar series; Cambridge
- 2018 University of Leicester, external seminar series; Leicester
- 2018 University of Glasgow, external seminar series; Glasgow
- 2019 Queen Mary University of London, external seminar series; London
- 2021 British microcirculation society (BMS) (online series)
- 2022 Greater Manchester Immunology Group's Seminar; Manchester
- 2022 Imperial College external seminar series; London
- 2022 Babraham Institute, external seminar series; Cambridge

List of publications

Recent publications; since 2016

1. Thornton EE and **Arnon TI**. It takes a village to skew a lymph node (2022) *Immunity* Oct 11;55(10):1751-1753. doi: 10.1016/j.immuni.2022.09.008.PMID: 36223721(Preview)
2. MacLean AJ, Richmond N, Koneva L, Attar M, Medina CAP, Thornton E, Cruz-Gomes A, El-Turabi A, Bachmann MF, Rijal P, Tan TK, Townsend A, Sansom SN, Bannard O, and **Arnon TI**. Secondary influenza challenge triggers resident memory B cell migration and rapid relocation to boost antibody secretion at infected sites (2022) *Immunity* Apr 12;55(4):718-733.e8. doi: 10.1016/j.immuni.2022.03.003.).

Using live imaging of explant lungs of influenza infected mice, we uncover cellular and molecular mechanisms that regulate local activation of resident memory B cells leading to rapid delivery of antibodies in a highly localized manner directly to sites of viral replication.

3. Chauveau A, Pirgova G, Cheng HW, De Martin A, Zhou FY, Wideman S, Rittscher J, Ludewig B, and **Arnon TI**. Visualisation of T cell migration in the spleen reveals a network of perivascular pathways that guide entry into T zones. (2020) *Immunity* 19;52(5):794-807. PMID: 32298648

We used cutting-edge intravital imaging approach that we developed to reveal novel paths and mechanisms of T cell entry into splenic T zones. The existence of an unknown egress sites is also revealed.

4. Pirgova G, Chauveau A, MacLean AJ, Cyster JG and **Arnon TI**. Marginal zone SIGN-R1+ macrophages are essential for the maturation of germinal centre B cells in the spleen. (2020) *PNAS* 18:201921673. PMID: 32424104

We developed a novel mouse model to selectively target marginal-zone macrophages in the spleen and demonstrated their function in promoting antibody responses.

5. Xie B, Khoyratty TE, Abu-Shah E, Cespedes P, MacLean AJ, Pirgova G, Zhiyuan Hu, Ahmed AA, Dustin ML, Udalova IA and **Arnon TI**. The zinc finger protein Zbtb18 inhibits differentiation of plasma cells by transcriptionally repressing class I PI3K subunits (J Immunol. 2021 Apr 1;206(7):1515-1527. doi: 10.4049/jimmunol.2000367.

We identified Zbtb18 as a novel transcriptional repressor that binds and inhibits expression of class I PI3K regulatory subunits, leading to suppression of plasma cell differentiation. The manuscript is currently under 3 months revision.

6. Reboldi A, **Arnon TI**, Rodda LB, Atakilit A, Sheppard D and Cyster JG. B cell interaction with subepithelial dendritic cells in Peyer's patches is critical for IgA production. (2016) *Science* 352(6287):aaf4822.

In this study we showed that IgA class switching in Peyer's patches in the gut is mediated by CCL6-dependent migration of activated B cells to the sub-endothelial dome (SED) and interactions with SED-resident dendritic cells. This process required lymphotoxin derived from innate lymphoid cells.

Additional first author publications

7. **Arnon TI** and Cyster JG. Blood, sphingosine-1-phosphate and lymphocyte migration dynamics in the spleen. (2014) *Current Topics in Microbiology and Immunology* 2014;378:107-28. PMID: 24728595. (Review).

This review provides a summary of the role of S1PR1 in lymphocyte migration in the spleen, the molecular mechanisms that regulate its activity and its importance for circulating as well as resident B cell positioning in the splenic environment.

8. **Arnon TI**, Horton BM, Grigorova IL and Cyster JG. Visualization of splenic marginal zone B cell shuttling and follicular B cell egress. (2013) *Nature* 493(7434):684-8. PMID: 23263181.

We report the first intravital imaging of cell movement in the splenic white pulp. We demonstrated that marginal-zone B cells are highly migratory and continuously oscillate between the marginal-zone and follicles and defined the egress path of follicular B cells from the spleen.

9. **Arnon TI**, Xu Y, Lo C, Pham T, An J, Coughlin S, Dorn GW, Cyster JG. GRK2-dependent S1PR1 desensitization is required for lymphocytes to overcome their attraction to blood. (2011) *Science* 333: 1898-903. PMID: 21960637.

We defined a new molecular requirement for lymphocyte movement from blood into lymph nodes and splenic follicles: we showed that desensitization of the egress receptor, S1PR1, is important to overcome distracting Gi-signals, allowing cells to appropriately respond to local chemokines and migrate into tissue.

10. **Arnon TI**, Kaiser JT, West AP, Jr., Olson R, Diskin R, Viertlboeck BC, Gobel TW, Bjorkman PJ. The crystal structure of CHIR-AB1: a primordial avian classical Fc receptor. (2008) *Journal of Molecular Biology* 381: 1012-24, PMID: 18625238.

11. **Arnon TI**, Markel G, Bar-Ilan A, Hanna J, Fima E, Benchetrit F, Galili R, Cerwenka A, Benharroch D, Sion-Vardy N, Porgador A, Mandelboim O. Harnessing Soluble NK Cell Killer Receptors for the Generation of Novel Cancer Immune Therapy. (2008) *PLoS One* 14;3(5):e2150. doi: 10.1371/journal.pone.0002150.

12. **Arnon TI** et al. Inhibition of the NKp30 activating receptor by pp65 of human cytomegalovirus. (2005). *Nature Immunology* 6: 515-23. PMID: 15821739.

We identified pp65, a cytomegalovirus tegument protein, as an antagonist that binds and inhibits NK cells by binding the lysis receptor NKp30. This work revealed a novel mechanism that allows cytomegalovirus to escape NK-mediated attack.

13. **Arnon TI**, et al. The mechanisms controlling the recognition of tumor- and virus-infected cells by NKp46. (2004) *Blood* 126: 664-72. PMID: 14504081
14. **Arnon TI***, Lev M*, Katz G, Chernobrov Y, Porgador A, Mandelboim O. Recognition of viral hemagglutinins by NKp44 but not by NKp30. (2001) *European Journal of Immunology* 31: 2680-9. PMID: 11536166. *With equal contribution.
15. **Arnon TI**, Markel G, Mandelboim O. Tumor and viral recognition by natural killer cells receptors. (2006) *Seminars in Cancer Biology* 16: 348-58. PMID: 16893656. (Review)

Additional selected co-author selected publications

16. Muppidi JR, **Arnon TI**, Bronevetsky Y, Veerapen N, Tanaka M, Besra GS, Cyster JG. Cannabinoid receptor 2 positions and retains marginal zone B cells within the splenic marginal zone. (2011) *Journal of Experimental Medicine* 208: 1941-8. PMID: 21875957.

We showed that cannabinoid receptor 2 is required to retain marginal-zone B cells in the spleen and to allow efficient antibody response to a CD1d-restricted systemic antigen.

17. Mandelboim O, Lieberman N, Lev M, Paul L, **Arnon TI**, Bushkin Y, Davis DM, Strominger JL, Yewdell JW, Porgador A. Recognition of haemagglutinins on virus-infected cells by NKp46 activates lysis by human NK cells. (2001) *Nature* 409: 1055-60. PMID: 11234016.

In this paper we identified the influenza hemagglutinin molecule as a novel ligand that binds and activates the NK lysis receptor NKp46, leading to killing of infected cells.

18. Gazit R, Gruda R, Elboim M, **Arnon TI**, Katz G, Achdout H, Hanna J, Qimron U, Landau G, Greenbaum E, Zakay-Rones Z, Porgador A, Mandelboim O. Lethal influenza infection in the absence of the natural killer cell receptor gene Ncr1. (2006) *Nature Immunology* 7: 517-23. PMID: 16565719.

Additional publications

19. Stern N, Markel G, **Arnon TI**, Gruda R, Wong H, Gray-Owen SD, Mandelboim O. Carcinoembryonic antigen (CEA) inhibits NK killing via interaction with CEA-related cell adhesion molecule 1. (2005) *Journal of Immunology* 174: 6692-701. PMID: 15905509.
20. Gonen-Gross T, Achdout H, **Arnon TI**, Gazit R, Stern N, Horejsi V, Goldman-Wohl D, Yagel S, Mandelboim O. The CD85J/leukocyte inhibitory receptor-1 distinguishes between conformed and beta 2-microglobulin-free HLA-G molecules. (2005) *Journal of Immunology* 175: 4866-74. PMID:16210588.
21. Markel G, Mussaffi H, Ling KL, Salio M, Gadola S, Steuer G, Blau H, Achdout H, de Miguel M, Gonen-Gross T, Hanna J, **Arnon TI**, Qimron U, Volovitz I, Eisenbach L, Blumberg RS, Porgador A, Cerundolo V, Mandelboim O. The mechanisms controlling NK cell autoreactivity in TAP2-deficient patients. (2004) *Blood* 103: 1770-8. PMID: 14604968.
22. Katz G, Gazit R, **Arnon TI**, Gonen-Gross T, Tarcic G, Markel G, Gruda R, Achdout H, Drize O, Merims S, Mandelboim O. MHC class I-independent recognition of NK-activating receptor KIR2DS4. (2004) *Journal of Immunology* 173: 1819-25. PMID: 15265913.

Referees

1. Professor Jason Cyster, University of California San Francisco, CA, USA Jason.Cyster@ucsf.edu, Lab Phone: +1 415-502-6638 (Postdoc supervisor)
2. Professor Wolfgang Kastenmuller, University of Wurzburg, Germany wolfgang.kastenmueller@uni-wuerzburg.de, Lab phone: +49 931 31-89740 (An independent international expert from my field)
3. Professor Anne Katherine (Katja) Simon, Max Delbrück Center for Moleculare Medicine (MDC), Berlin, German katja.simon@mdc-berlin.de, Lab phone: +49 30 9406-0 (a former senior colleague from the Kennedy Institute)