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Our life companions: the human follicular mite *Demodex folliculorum**

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We carry them in our skin pores through our entire life, from birth to death. We offer them shelter and in return, they tidy-up our pores. We go on with our busy day life and they sleep. They wake up when we go to sleep and while we are deeply dreaming, they move around, visit other pores and mates, and reproduce. Despite being our ‘very own’ life companions, until recently, we knew very little about their struggle.

Their miniaturised Bauplan is perfectly fit for life inside the pores of hair follicles and sebaceous glands. Perception of light is achieved by one of the smallest ‘eyes’ (photoreceptors) known to date, and movement and dispersal is accomplished by minute legs powered by just three unicellular-uninucleate muscle segments. With a unique arrangement of *Hox* genes, their reproductive organs allow them to mate and to deliver offspring inside the limited space offered by the pores.

Unless they soon find a way out, genome erosion, on an evolutionary time scale, is leading them to a dead end, to extinction. They outbreed less and less: each of us has a unique population, started by a few colonisers, legacy of our moms when we were babies. This resulted in a mite species that presents the lowest number of protein genes. Yet, they manage to successfully carry on with their lives by synchronising with our lifestyles, and we hope they will keep doing it for the foreseeable future!

Demodex folliculorum (Prostigmata, Demodecidae) has adapted to the life in the human pores and the circadian rhythm of their host (Smith *et al.*, 2022). The difference between an ectosymbiont and a pathogen lies in the numbers. The amount of *Demodex* mites on healthy human faces is controlled by several factors.

First, the physical size of the pores. The older a person gets, the wider the pores become and the more mites a pore can accommodate (Zeytun, 2017; El Bassiouni *et al.*, 2005). Pore size also increases with inflammation and with it *Demodex* (Casas *et al.*, 2012; Karabay and Çerman, 2020; Forton and De Maertelaer, 2021).

Second, the physiology, the feeding of the mites. The mites feed on sebum produced inside the pores. Sebum production is the highest in the age range of 20 to 30 years (Foley *et al.*, 2021).

The immune system of a healthy person seems to control the density of *Demodex*. This becomes evident in various ways.

Suppression of cellular immunity by cancers might lead to increase in *Demodex* numbers or to abnormal antiparasitic attacks of the immune system on *Demodex* (Seyhan *et al.*, 2004; Bakacak *et al.*, 2020; Zijsa-Sołtys *et al.*, 2021). Immunosuppressive viruses such as HIV I can lead to an increase of *Demodex* (Yamaoka *et al.*, 2014; Grigoryan *et al.*, 2018; Trama *et al.*, 2018). Iatrogenic induced immunosuppression for the treatment of autoimmune diseases, essential thrombocytosis, Crohn’s disease, psoriasis, Cushing’s syndrome and neoplasms, and for the support of organ transplantation support demodicosis/demodicidosis (Amitay-Laish *et al.*, 2022). Autoimmune diseases themselves in the form of failure of the thyroid in humans and dogs or in rheumatoid arthritis can lead to breakdown of the host’s regulation of *Demodex* density (Pinsenschaum *et al.*, 2019; Yazisiz *et al.*, 2020; Dursun *et al.*, 2022). From alcoholism to heart failure, if homeostasis is compromised, *Demodex* increases (Kokaçya *et al.*, 2016; Yüksel and Yüksel, 2020; Pormann *et al.*, 2021). This are all cases of secondary demodicosis.

The older clinical literature on demodicosis in humans and dogs argues that *Demodex* suppresses the host

immune system and therefore leads to the clinical manifestations. These reports fail to explain why or how *Demodex* persists in healthy humans and dogs.

Bit by bit, mechanisms of immune dysregulation are being discovered that lead to pathological levels of *Demodex*. Paediatric demodicosis, chronic demodicosis, and demodicosis as part of rosacea in humans is caused by a *Signal transducer and activator of transcription (STAT) 1* heterozygous gain-of-function (GOF) mutations eventually leading to excessive interferon γ response and compromised T helper cell 17 differentiation (Second *et al.*, 2017; Molho-Pessach *et al.*, 2020; Saez-de-Ocariz *et al.*, 2020; Baghdad *et al.*, 2021; Martinot *et al.*, 2021; Shamriz *et al.*, 2021; Zhang *et al.*, 2021).

Demodex is controlled by its host through innate type 2 immunity (Ricardo-Gonzalez *et al.*, 2022). This raises the question whether primary demodicosis in humans exists at all.

References

- Amitay-Laish, I., Solomon-Cohen, E., Feuerman, H., Didkovsky, E., Davidovici, B., Leshem, Y.A., Pavlovsky, L., Reiter, O., Mimouni, D., Hodak, E. & Segal, R. (2022) Facial demodicosis in the immunosuppressed state: A retrospective case series from a tertiary referral center. *International Journal of Dermatology*, 61, 1245–1252.
<https://doi.org/10.1111/ijd.16162>
- Baghad, B., El Fatoiki, F.Z., Benhsaien, I., Bousfiha, A.A., Puel, A., Migaud, M., Chiheb, S. & Ailal, F. (2021) Pediatric demodicosis associated with gain-of-function variant in STAT1 presenting as rosacea-type rash. *Journal of Clinical Immunology*, 41, 698–700.
<https://doi.org/10.1007/s10875-020-00942-z>
- Bakacak, Z., Kaplanoglu, M., Bakacak, M. & Çelik, T. (2020) *Demodex folliculorum* mite infestation in gynecological cancers: A case control study. *European Journal of Gynaecological Oncology*, 41, 583–586.
<https://doi.org/10.31083/j.ejgo.2020.04.3687>
- Casas, C., Paul, C., Lahfa, M., Livideanu, B., Lejeune, O., Alvarez-Georges, S., Saint-Martory, C., Degouy, A., Mengeaud, V., Ginisty, H., Durbise, E., Schmitt, A.M. & Redoules, D. (2012) Quantification of *Demodex folliculorum* by PCR in rosacea and its relationship to skin innate immune activation. *Experimental Dermatology*, 21, 906–910.
<https://doi.org/10.1111/exd.12030>
- Dursun, A.T., Bayramgürler, D., Demirsoy, E.O., Aktürk, A.S., Kiran, R. & Sayman, N. (2022) Could there be an association between Hashimoto's thyroiditis and demodex infestation? *Journal of Cosmetic Dermatology*.
<https://doi.org/10.1111/jocd.15005>
- El Bassiouni, S.O., Ahmed, J.A.A., Younis, A.I., Ismail, M.A., Saadawi, A.N. & Bassiouni, S.O. (2005) A study on *Demodex folliculorum* mite density and immune response in patients with facial dermatoses. *Journal of the Egyptian Society of Parasitology*, 35, 899–910.
- Forton, F.M.N. & De Maertelaer, V. (2021) Which factors influence *Demodex* proliferation? A retrospective pilot study highlighting a possible role of subtle immune variations and sebaceous gland status. *Journal of Dermatology*, 48, 1210–1220.
<https://doi.org/10.1111/1346-8138.15910>
- Foley, R., Kelly, P., Gatault, S. & Powell, F. (2021) *Demodex*: A skin resident in man and his best friend. *Journal of the European Academy of Dermatology and Venereology*, 35, 62–72.
<https://doi.org/10.1111/jdv.16461>
- Grigoryan, O.M., Moskvina, T.V., Sklyar, L.F., Galkina, I.V., Beniova, S.N. & Shchelkanov, M.Y. (2018) [Demodicosis in HIV-infected patients]. *Meditinskaya Parazitologiya i Parazitarnye Bolezni*, 2018, 50–57.
<https://doi.org/10.33092/mp2018.3.50-57>
- Karabay, E.A. & Çerman, A.A. (2020) *Demodex folliculorum* infestations in common facial dermatoses: Acne vulgaris, rosacea, seborrheic dermatitis. *Anais Brasileiros de Dermatologia*, 95, 187–193.
<https://doi.org/10.1016/j.abd.2019.08.023>
- Kokaçya, M., Kaya, Ö., Çöpođlu, Ü. & Elmaciođlu, S. (2016) Prevalence of *Demodex* spp among alcohol-dependent patients. *Cukurova Medical Journal*, 41, 259–263.
<https://doi.org/10.17826/cutf.203543>
- Martinot, M., Korganow, A.S., Wald, M., Second, J., Birckel, E., Mahe, A., Souply, L., Mohseni-Zadeh, M., Droy, L., Tarabeux, J., Okada, S., Migoud, M., Puel, A. & Guffroy, A. (2021) Case report: a new gain-of-function mutation of STAT1 identified in a patient with chronic mucocutaneous candidiasis and rosacea-like demodicosis: an emerging association. *Frontiers in Immunology*, 12, e760019.
<https://doi.org/10.3389/fimmu.2021.760019>
- Molho-Pessach, V., Meltser, A., Kamshov, A., Ramot, Y. & Zlotogorski, A. (2020) STAT1 gain-of-function and chronic demodicosis. *Pediatric Dermatology*, 37, 153–155.
<https://doi.org/10.1111/pde.14011>

- Pinsenschaum, L., Chan, D.H.L., Vogelnest, L., Weber, K. & Mueller, R.S. (2019) Is there a correlation between canine adult-onset demodicosis and other diseases? *Veterinary Record*, 185, 729.
<https://doi.org/10.1136/vr.105388>
- Pormann, A.N., Vieira, L., Majolo, F., Johann, L. & da Silva G.L. (2021) *Demodex folliculorum* and *Demodex brevis* (Acari: Demodicidae) and their association with facial and non-facial pathologies. *International Journal of Acarology*, 47, 396–403.
<https://doi.org/10.1080/01647954.2021.1919757>
- Ricardo-Gonzalez, R.R., Kotas, M.E., O’Leary, C.E., Singh, K., Damsky, W., Liao, C., Arouge, E., TenVooren, I., Marquez, D.M., Schroeder, A.W., Cohen, J.N., Fassett, M.S., Lee, J., Daniel, S.G., Bittinger, K., Diaz, R.E., Fraser, J.S., Ali, N., Ansel, K.M., Spitzer, M.H., Liang, H.-E. & Locksley, R.M. (2022) Innate type 2 immunity controls hair follicle commensalism by *Demodex* mites. *Immunity*, 55, 1891–1908.e12
<https://doi.org/10.1016/j.immuni.2022.08.001>
- Sáez-de-Ocariz, M., Suárez-Gutiérrez, M., Migaud, M., Farrill-Romanillos, O.P., Casanova, J.L., Segura-Mendez, N.H., Orozco-Covarrubias, L., Espinosa-Padilla, S.E., Puel, A. & Blancas-Galicia, L. (2020) Rosacea as a striking feature in family members with a STAT1 gain-of-function mutation. *Journal of the European Academy of Dermatology and Venereology*, 34, e265–e267.
<https://doi.org/10.1111/jdv.16241>
- Second, J., Korganow, A.-S., Jannier, S., Puel, A. & Lipsker, D. (2017) Rosacea and demodicidosis associated with gain-of-function mutation in STAT1. *Journal of the European Academy of Dermatology and Venereology*, 31, e542–e544.
<https://doi.org/10.1111/jdv.14413>
- Seyhan, M.E., Karıncaoğlu, Y., Bayram, N., Aycan, O. & Kuku, I. (2004) Density of *Demodex folliculorum* in haematological malignancies. *Journal of International Medical Research*, 32, 411–415.
<https://doi.org/10.1177/147323000403200410>
- Shamriz, O., Lev, A., Simon, A. J., Barel, O., Javasky, E., Matza-Porges, S., Shaulov, A., Davidovics, Z., Toker, O., Somech, R., Zlotogorski, A., Molho-Pessach, V. & Tal, Y. (2021) Chronic demodicosis in patients with immune dysregulation: An unexpected infectious manifestation of *Signal transducer and activator of transcription (STAT)1* gain-of-function. *Clinical and Experimental Immunology*, 206, 56–67.
<https://doi.org/10.1111/cei.13636>
- Smith, G., Manzano-Marin, A., Reyes-Prieto, M., Antunes, C.S.R., Ashworth, V., Goselle, O. N., Jan, A.A.A., Moya, A., Latorre, A., Perotti, M.A. & Braig, H.R. (2022) Human follicular mites: Ectoparasites becoming symbionts. *Molecular Biology and Evolution*, 39, msac125.
<https://doi.org/10.1093/molbev/msac125>
- Trama, I.C., Arévalo, J., Alvarado, M.E. & Balaña, G.E. (2018) Rosácea granulomatosa en paciente HIV. A propósito de un caso. [Granulomatous rosacea in HIV patient. A case report.] *Revista Argentina de Dermatología*, 99, 71–80.
- Yamaoka, T., Murota, H., Tani, M. & Katayama, I. (2014) Severe rosacea with prominent *Demodex folliculorum* in a patient with HIV. *Journal of Dermatology*, 41, 195–196.
<https://doi.org/10.1111/1346-8138.12352>
- Yazısız, H., Çekin, Y., Sezer, Y., Bostan, F. & Koçlar, F.G. (2020) *Demodex* species frequency and risk factors in patients with rheumatoid arthritis. *Archive of Rheumatology*, 35, 376–384.
<https://doi.org/10.46497/ArchRheumatol.2020.7699>
- Yüksel, S. & Yüksel, E.P. (2020) Increased *Demodex* density in patients hospitalized for worsening heart failure. *Journal of Personalized Medicine*, 10, e39.
<https://doi.org/10.3390/jpm10020039>
- Ziaja-Sołtys, M., Kołodziejczyk, M., Rymgajło-Jankowska, B., Wróbel-Dudzińska, D., Suchodoła-Ratajewicz, E., Szlonzak, D., Żarnowski, T. & Bogucka-Kocka, A. (2021) Massive demodicosis of the eyes in a patient with Sjögren syndrome: A case report. *Acta Parasitologica*, 66, 677–681.
<https://doi.org/10.1007/s11686-020-00297-w>
- Zeytun, E. (2017) *Demodex* (Acari: Demodicidae) infestation in the elderly and its relationship with the skin parameters such as moisture, pH, and temperature: A cross-sectional study. *Turkish Journal of Geriatrics*, 20, 142–150.
- Zhang, W., Chen, X., Gao, G., Xing, S., Zhou, L., Tang, X., Zhao, X. & An, Y. (2021) Clinical relevance of Gain- and Loss-of-Function germline mutations in STAT1: A systematic review. *Frontiers in Immunology*, 12, e654406.
<https://doi.org/10.3389/fimmu.2021.654406>