Topic 3 - External factors affecting transmission and monitoring.

- DFTD spread is affected by devil density, which is affected by traversal ability (geographical conditions), food availability. There is preliminary research on seasonal changes.

DFTD spreads to where devils go and spreads around faster depending on high devil densities. (Cunningham et. al; 2021:Figure 3a) shows the low devil density found within most of the western regions of Tasmania. Devil density may be affected by the troubles associated with traversal in dense mosaics of biomes (McCallum et. al; 2007; para 2 after figure 2) like that found in the West, with the found mountains and rainforests likely hampering easy travel. The land found within the East and Centre of Tasmania consists of flatter land, grassy woodlands, dry forests, and heathland (Kitcehener A and Harris; 2013 and Cunningham et. al; 2021), permitting easier traversal and therefore higher devil density. This indicates that the reason DFTD spread from the first recorded case in the North-East (cite this) to the South-East faster than East-West (McCallum et. al; 2007 and Cunningham et. al; 2021) is due to higher devil densities and traversal opportunities. It may be years until the low density and remote South-West region of Tasmania is overrun with DFTD due to the geography (McCallum et. al; 2007 para 2 after section heading ‘Distribution and Spread of Disease’).

- 2007 article (McCallum et. al; 2007) believed that it would take 3-20 years to be country-wide and 3-10 years to reach the isolated north-west population of devils.

- Devils live in a ~20km^2 area, traversing 6-7km/day. A significant reason for why devils may move around or out of their territory is for mating rituals, which happens regardless of devil density (Cunningham et. al; 2021; para 6)

- 1996 primary populations were in Central/North-East/North-West (~2, max 3.5 devils/km^2). 2019 primary population was in North-West (2, max 3.5 devils/km^2) with the next most being in West and Central (1.5-1, max 1.5 devils/km^2 respectively). (Cunningham et. al; 2021: figure 4a)

- Devils density also depends on food availability (Woods et. al; 2018:“Monitoring the spread of DFTD”, para. 4)

- Seasonal changes (Raven N et. Al 2022:4.2)

- Higher immune gene expression in mostly Summer and sometimes Winter

- It is unknown whether these increased immune gene responses affect the ability of Tasmanian Devils to fight DFTD. “There’s too many darn unknowns”.

- Monitoring difficulties (not finding any infected devils in suspected regions, difficulty in diagnosing tumours as misc. wounds look similar)

- The public is helping report to a service known as the STDP (Save the Tasmanian Devil Program) of roadkill and other sightings of devils with DFTD

- Which you can do to at… (hotline, website?)

- Uncovered DFTD1 cases further west than the known disease-front

- First case of DFTD2 was recorded

- Motion sensing cameras (Woods et. al; 2018) that record only when motion is detected. They are setup with meat, luring canisters containing attractive smells, memory cards, and batteries that last two months.

- Less devils as time goes (meat loss, lures lose their smell)

- 2D images, differing conditions per photo, and the inability to adjust the view make distinguishing DFDT from wounds, scar tissue, and fresh wounds difficult and occasionally impossible (tumour may be only in their mouth)

- Increase the probability of seeing devils compared to more lure/manual release traps

- Wounds looking similar (<https://pubmed.ncbi.nlm.nih.gov/21383118/> - Abstract), ways to differentiate

- Tests for expression of Periaxin - shows specificity for Schwann cells and works as a tool for detecting DFTD cells (immunosenescence)

Gene regulation in immune cells ->

- All mammals individually experience a changing immunity over time, known as immunosenescence (Judson et. al; 2020) found through immune gene expression profiling of blood samples (Raven N et. al; 2022)

- Adaptive immunity decreases over time

- Age-related immunity changes can increase the risk of developing cancers

- Expand on Periaxin

- Expression of immune genes in blood may be affected by seasons, age, and sex. These can be further modified by DFTD infections. (Raven N et. al; 2022)

- Immune genes that have their expression rates changed influence immune system responses and their expression rates are more likely to be inherited by a following generation. (Fairfax and Knight; 2014). This idea of immunity improving over generations is **supported by something** – devil immunity is slowly improving

- Autumn/Spring significantly lowers 10 gene’s expression rates in comparison to Summer; Age displays significantly less expression for 2 genes (Raven N et. Al 2022:results)

- Seasonal changes in immune expression are guessed to be related to managing optimal breeding times vs the maintenance of the immune system (Raven N et. Al 2022; Discussion 4.2, para 1)

- All that said, it is unknown what part of the seasonal changes actually affect the immune expressions and it is unknown if they affect the Devil’s abilities to fight DFTD (Raven N et. Al 2022; Discussion 4.2, para 2). More research is needed.

- Relationships are complicated and not always clear – Cells and Genes people know what’s up

- The CD16 receptor expressions levels have an independent and strong positive correlation with DFTD contraction. This needs more research before drawing conclusions about whether it is a boon or hindrance to the immune system fighting DFTD. It is also theorised that CD16 could be used similarly to periaxin – a biomarker to find DFTD cases.

Over the last decade devils have begun to show adaptations to the disease (Epstein et al., [2016](https://onlinelibrary.wiley.com/doi/10.1111/mec.16408#mec16408-bib-0038)), devils surviving longer with visible tumours (Wells et al., [2017](https://onlinelibrary.wiley.com/doi/10.1111/mec.16408#mec16408-bib-0149)) and tumour regressions occurring in some populations (Pye, Hamede, et al., [2016](https://onlinelibrary.wiley.com/doi/10.1111/mec.16408#mec16408-bib-0107)). Importantly, some of the devils with tumour regressions have showed modifications in the activation of tumour suppressor genes (Margres et al., [2020](https://onlinelibrary.wiley.com/doi/10.1111/mec.16408#mec16408-bib-0084)). (DOI mec)

Conclusion: “Based on the persistence of devils at all long-term diseased sites, our model predicts the overall population is likely to stabilise within the next 10 years. This supports recent simulations suggesting the most likely long-term outcomes are either the coexistence of devils and DFTD, or DFTD fading out (Wells et al. 2019), with genomic evidence suggesting a transition towards endemism” (Cunningham et. al; 2021: Discussion, ‘Population trends and conservation’ para 2)

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7121369/> (Section: DFTD Pathogenesis) -> “Mortality results when large primary tumours obstruct feeding, leading to starvation, or from complications associated with metastasis (Pyecroft et al., [2007](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7121369/#CR63)).”

Articles to checkout (search was: ‘dftd external factors "cancer" "Tasmanian devil"’):

Article 1 -> Raven N, Klaassen M, Madsen T, Thomas F, Hamede R K, and Ujvari B; (2022); ‘Transmissible cancer influences immune gene expression in an endangered marsupial, the Tasmanian devil (Sarcophilus harrisii)’; *Molecular Ecology*; 31(8):2293-2311; <https://doi.org/10.1111/mec.16408>

(Raven N et. Al 2022)

Article 5 -> Woods G M, Fox S, Flies A S, Tovar C D, Jones M, Hamede R, Pemberton D, Lyons A B, and Bettiol S S; (2018); ‘Two Decades of the Impact of Tasmanian Devil Facial Tumor Disease’; *Integrative & Comparative Biology*; 58(6):1043-1054; <https://doi.org/10.1093/icb/icy118>

(Woods et. al; 2018)

Article 6 -> McCallum H, Tompkins D M, Jones M, Lachish S, Marvanek S, Lazenby B, Hocking G, Wiersma J, and Hawkins C E; (2007); ‘Distribution and Impacts of Tasmanian Devil Facial Tumor Disease’; *EcoHealth*; 4:318-325; <https://doi.org/10.1007/s10393-007-0118-0>

(McCallum et. al; 2007)

Article 7 -> Cunningham C X, Comte S, McCallum H, Hamilton D G, Hamede R, Storfer A, Hollings T, Ruiz-Aravena M, Kerlin D H, Brook B W, Hocking G, Jones M E; (2021); ‘Quantifying 25 years of disease-caused declines in Tasmanian devil populations: host density drives spatial pathogen spread’; *Ecology Letters*; 24(5):958-969; <https://doi.org/10.1111/ele.13703>

(Cunningham et. al; 2021)

Article 8 <https://nre.tas.gov.au/conservation/flora-of-tasmania/from-forest-to-fjaeldmark-descriptions-of-tasmanias-vegetation>

Kitcehener A and Harris S; (2013); *From Forest to Fjaeldmark​: Descriptions of Tasmania's Vegetation (Edition 2).* Department of Primary Industries, Parks, Water and Environment

(Kitcehener A and Harris; 2013)

<https://nre.tas.gov.au/conservation/flora-of-tasmania/from-forest-to-fjaeldmark-descriptions-of-tasmanias-vegetation> (Introduction - Page 21 - Geographical and environmental context) - Government of Tasmania (<https://nre.tas.gov.au/Documents/f2f_forest_fjaeldmark.pdf>)

Article 9 -> Judson J M, Reding D M, and Bronikowski A M; (2020); ‘Immunosenescence and its influence on reproduction in a long-lived vertebrate’; *Journal of Experimental Biology*; 223(12); <https://doi.org/10.1242/jeb.223057>

(Judson et. al; 2020)

Article 11 -> Fairfax B P and Knight J C; (2014); ‘Genetics of gene expression in immunity to infection’; *Current Opinion in Immunology*; 30:63-71; <https://doi.org/10.1016/j.coi.2014.07.001>

(Fairfax and Knight; 2014)

Info about DFTD transmission: Article 2 [www.doi.org/10.1007/s00018-019-03435-4](http://www.doi.org/10.1007/s00018-019-03435-4) - Curse of the devil: molecular insights into the emergence of transmissible cancers in the Tasmanian devil (Sarcophilus harrisii)

Strength of DFTD and divergences: Article 3 [www.doi.org/10.1371/journal.pbio.3000926](http://www.doi.org/10.1371/journal.pbio.3000926) - Evolution and lineage dynamics of a transmissible cancer in Tasmanian devils

Very interesting read -> DFTD1 vs. DFTD2 (origins, differences, devil predispositions - risk factors): Article 4 [www.doi.org/10.1007/s00018-019-03259-2](http://www.doi.org/10.1007/s00018-019-03259-2) - Two of a kind: transmissible Schwann cell cancers in the endangered Tasmanian devil (Sarcophilus harrisii)

Info about IGa: Article 10 - <https://www.google.com/search?client=firefox-b-d&q=Immunoglobulin+A> (fights off sickness in mucous membranes)

Immunosenescene:

So as one gene activates less, another may or may not increase. This could lead to the same, a less effective, or preferably, a more effective immune response within the Devil. The Raven et. al study studied 16 out of 141 (Morris et. al; 2015) immune genes within the Devil

Morris K M, Cheng Y, Warren W, Papenfuss A T, and Belov K

<https://bmcgenomics.biomedcentral.com/articles/10.1186/s12864-015-2206-9>