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TH-OR47

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Background: Social media platforms are used in contemporary crowdsourcing, and Twitter is apt for reaching a large number of people with a common interest. Users, especially those with a small follower count may find it challenging to reach a large audience. #AskRenal was developed as a Twitter crowdsourcing tool to help users get answers to nephrology questions. We hypothesized that the #AskRenal hashtag could be used by anyone to receive helpful and timely responses to simple or complex nephrology questions posed on the social media platform.

Methods: A Twitter account @AskRenal, and an online Twitter bot that automatically retweeted any new tweets containing the hashtag #AskRenal were created. Using the Symplur Healthcare Hashtag tool, we extracted and analyzed public Twitter content containing the hashtag #AskRenal posted between Dec 2016 to Aug 2020. Tweets were excluded if they were duplicates, retweets, or if the tweet content was not the form of an original question. A group of 15 medical professionals reviewed #AskRenal tweets individually and a 10-question survey was completed for each one.

Results: During the study period, there were 17,704 tweets containing the hashtag #AskRenal and 3099 were included in the survey analysis. We found that 40% (1228/3099) of #AskRenal questions were posed by users with < 1000 followers and 9% (270/3099) were from students and trainees. The questions were spread across a wide range of nephrology topics. Over 75% (2386/3099) of the #AskRenal questions garnered a response, and answers came quickly with 69% (1644/2386) receiving a reply within 6 hours of posting. The reviewers found these responses to be helpful in answering the original questions 83% (1978/2386) of the time. The inclusion of hyperlinks and images in the reply was associated with a helpful answer ($p < 0.001$) and a higher follower count was not significantly associated with the probability of obtaining a helpful answer.

Conclusions: We demonstrated that a targeted hashtag and a dedicated Twitter account that retweets the hashtag automatically can be used to garner timely and helpful responses by a wide range of individuals, irrespective of follower count, seeking answers to nephrology questions.

TH-OR48

Using Three-Dimensional Imaging and Single-Cell Transcriptomics to Interrogate Human Kidney Lymphatics in Transplant Rejection

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Background: Lymphatics participate in immune homeostasis and their dysfunction has been linked to autoimmunity and cancer. There is a need to enhance our understanding of the spatial and molecular features of lymphatics in human kidney health and transplant rejection.

Methods: Wholemount immunolabelling, tissue clearing and 3D microscopy were used to visualise lymphatics in non-transplanted donor kidney and allografts with chronic transplant rejection (CKTR). Furthermore, we integrated multiple human kidney single-cell RNA sequencing (scRNA-seq) datasets, including samples with distinct aetiologies of CKTR.

Results: In donor kidneys, lymphatics reside hierarchically within the cortex, form terminal branches along cortical nephron segments and possess a unique capillary phenotype, which is distinct from other organ lymphatics due to their low expression of LYVE1. In CKTR, lymphatics undergo expansion, lose structural hierarchy and infiltrate the medulla (**Fig.1**). Allograft lymphatics are predominantly donor-derived, express HLA-DR, and exhibit C4d immunoreactivity; indicative of targetting by anti-allograft antibodies. Additionally, kidney lymphatics are T cell-rich conduits which interconnect tertiary lymphoid structures. Using scRNA-seq, we identify putative crosstalk between lymphatics and T cells, featuring co-inhibitory immune checkpoints.

Conclusions: Utilising 3D imaging and scRNA-seq, we uncovered the spatial and molecular profile of human kidney lymphatics. We have revealed fundamentals of these vessels to inform future studies into renal biology, as well as identifying lymphatic phenomena and molecular candidates involved in CKTR.

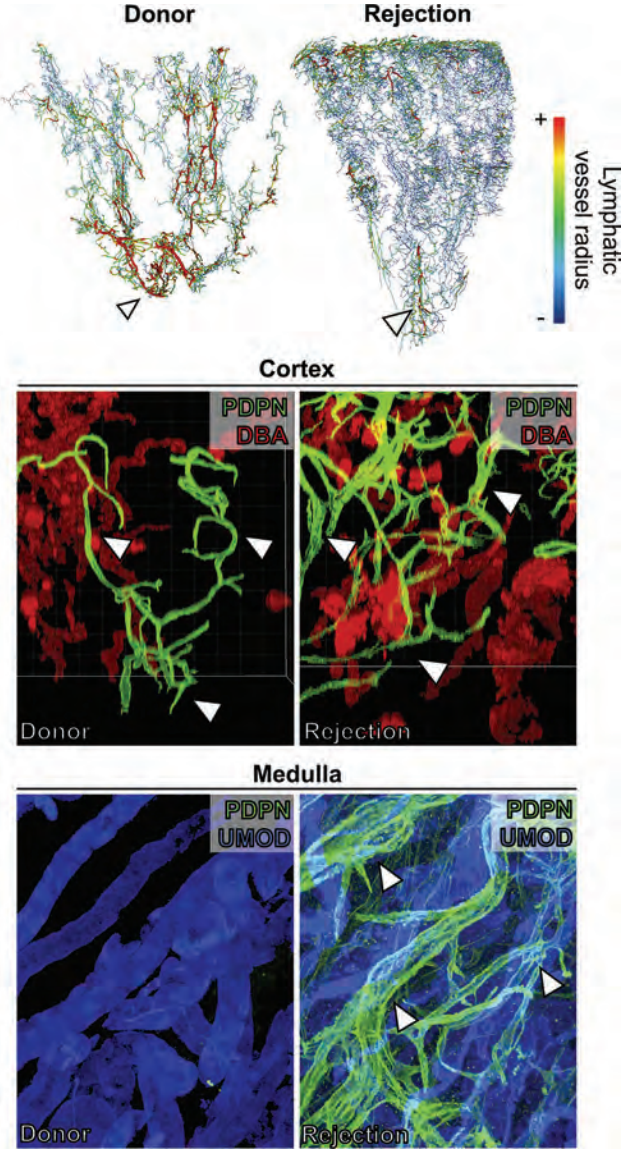

Fig.1. The lymphatic phenotype in transplant rejection

TH-OR49

Critical Role of CD74 in Immune Regulation and Allograft Tolerance

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Background: While known as the receptor for Microphage Inhibitory Factor (MIF) and MHC class II chaperone, the role of CD74 remains elusive in alloimmunity. We identified enriched CD74 transciptome in urinary exosome of kidney allograft rejection, thus we explored the role of CD74 in alloimmune response in a mice transplant model.

Methods: We generated universal and conditional CD74KO mice and used as recipients of murine heart allograft ina full HLA mismatch model. Graft survival assessed; with Immunophenotyping of allograft and proliferation and functional assays performed.

Results: We observed indefinite survival heart allografts in CD74KO recipients compared to WT (MST >100 vs 7 days, p=0.0008); Treg depletion resulted in allograft rejection (Fig 1,2). At day 7 post-transplantation, 5 times increase in Tregs infiltrating allograft as compared to WT noted, similar pattern with smaller magnitude observed in draining lymph node. To our suprise, higher frequency of activated effector CD4 cells (CD44+) observed in allograft of CD74KO recipients. In-vitro, activated effector CD4 cells harvested from CD74KO mice revealed decreased proliferation compared to WT. In contrast, CD74KO Tregs showed higher proliferation and suppressive function in-vitro. Naive CD4 cells show minimal CD74 expression. CD74 expression significantly increased in Tregs upon stimulation at both protein and RNA level (up to 30 times), with minimal MIF expression. Effector CD4 cells show 8 times increase in MIF expression. MIF is involved in activation of CD4 cells and we are currently studying its role in supression of Treg activity adn function.