Dendritic cell
Fibroblastic reticular cell
Lymphocyte
LTβ
CLEC-2
Inhibition of contraction
Stretching
Proliferation
Maturation of precursors
Survival signals
Migration
Activation
Proliferation

Cell migration
Inhibition of contraction
Stretching
Proliferation
Maturation of precursors
Survival signals
Migration
Activation
Proliferation

Steady state
Acute Inflammation
Chronic Inflammation

1) Dendritic cells in close contact with FRC network
2) Dendritic cells provide LTβ to maintain FRC network
3) FRCs form interconnected contractile scaffold

1) Increased numbers of Dendritic cells, increased CLEC-2 available
2) Influx of naive lymphocytes
3) Dendritic cells present antigen and activate T cells
4) T cell proliferation induces strain on FRC network
5) PDPN on FRCs is inhibited by CLEC-2 allowing stretching

1) Reduced numbers of DCs
2) Increased number of FRCs allows further LN expansion
3) FRC proliferation and/or recruitment of FRC precursors
4) Reduced CLEC-2 allows return of FRC contractility
5) Chronic proliferation results in over-production of extracellular matrix
1) Lymphocyte recruitment

2) Compromised barrier function

3) Leakage of platelets

4) Binding PDPN+ FRCs activates CLEC-2 to release S1P from platelets

5) S1P acts on endothelium to strengthen cell-cell adhesions

6) Vascular integrity maintained

1) Dendritic cells in close contact with FRC network

2) FRCs in close contact with blood vessels

3) Dendritic cells secrete LTβ to activate LTβR on FRCs

4) FRCs secrete VEGF to maintain and regulate endothelial cells

5) S1P acts on endothelium to strengthen cell-cell adhesions

6) Vascular integrity maintained

Steady state

Inflammation

Cell-cell communication

Platelets

Fibroblastic reticular cell

Blood endothelium

Lymphocyte

Dendritic cell

PDPN

CCL19

CCL21

LTβ

IL-7

ICAM-1

S1P

VEGF

Cell migration

Cell adhesion
Growth factor production

Cell cell adhesion
Proliferation

Survival signals
Migration and recruitment