Role of CD38/cyclic ADP-ribose Signaling in Human Asthma

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Background

- Asthma is a human disorder of the airway characterized by airway hyper-responsiveness, inflammation, and airway obstruction.
- Abnormal contraction of the smooth muscle in the airways is an important cause of the reversible obstruction to airflow.
- Smooth muscle contraction is caused by intracellular calcium release from the sarcoplasmic reticulum (SR).
- CD38 is a trans-membrane protein that converts β-NAD to cyclic ADP-ribose (cADPR). cADPR mobilizes calcium ions from the SR.
- CD38 expression has been linked to pathogenesis of asthma in mice.

Aim of the Study

To determine the expression of CD38 in asthmatic HASM cells.

Hypothesis

CD38 expression will be elevated in asthmatic HASM cells compared to non-asthmatic ASM cells.

Results

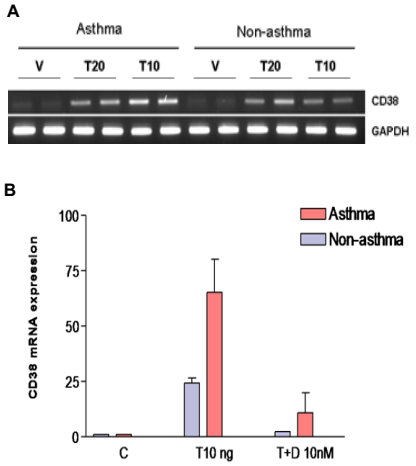
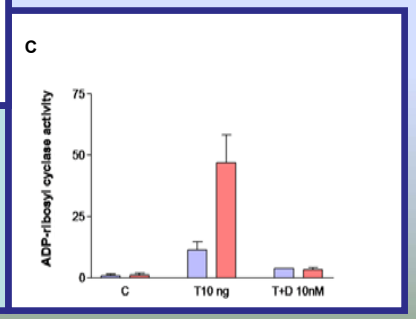
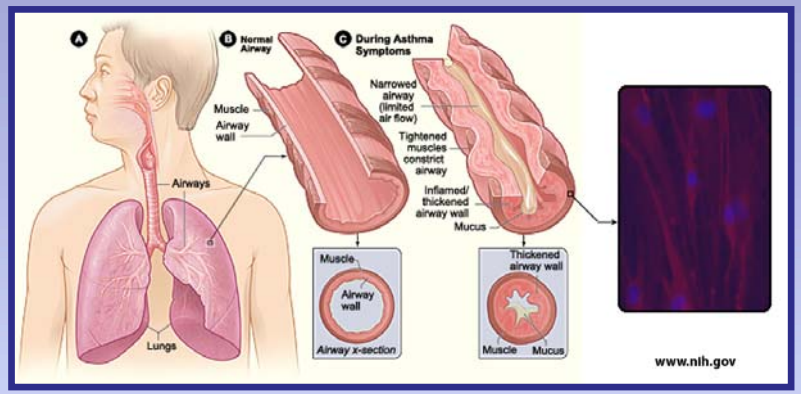
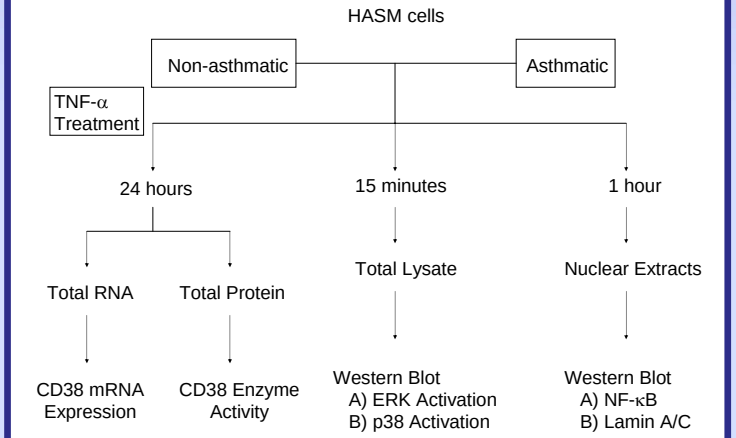


Fig 1. TNF-α-induced CD38 Expression in asthmatic HASM cells. A): there was no constitutive expression of CD38 in asthmatic or non-asthmatic cells. B) and C): TNF-α induced higher levels of CD38 expression in asthmatic HASM cells compared to non-asthmatic cells. CD38 expression was similarly inhibited by the anti-inflammatory drug dexamethasone in asthmatic and non-asthmatic cells (n=3-6/group).







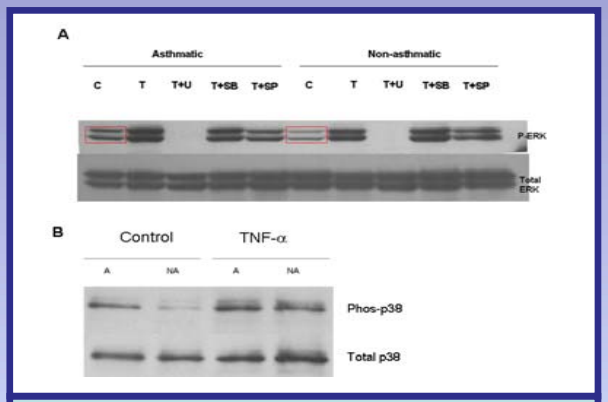


Fig 2. MAPK Activation in Asthmatic HASM cells. A) ERK1/2 and B) p38 MAPK showed increased basal and TNF-α-induced activation in asthmatic cells compared to non-asthmatic cells. (Blots representative of 3 experiments.)

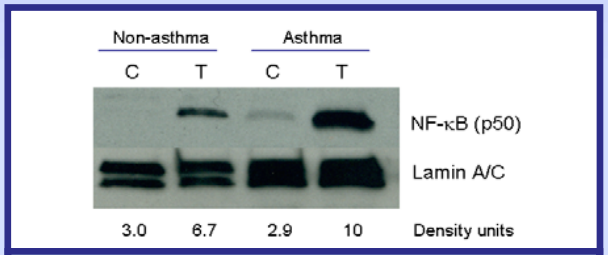


Fig 3. TNF-α-induced activation of NF-κB in Asthmatic HASM cells. Nuclear translocation of NF-κB in response to TNF-α was determined. The cytokine-induced NF-κB translocation was slightly higher in asthmatic HASM cells compared to the non-asthmatic cells. (Blot representative of 2 experiments.)

Conclusions

1. There is no constitutive expression of CD38 in asthmatic HASM cells.
2. TNF-α induces higher level of CD38 expression in asthmatic HASM cells compared to non-asthmatic cells.
3. The likely mechanism of differentially elevated CD38 expression in asthmatic cells is transcriptional regulation.

Future Directions

Determining cellular Ca^{2+} elevation in asthmatic cells in response to contractile agonists. We expect to find higher Ca^{2+} transients in asthmatic cells compared to the non-asthmatic cells.

Acknowledgments

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