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A mathematical model of calcium dynamics in airway smooth muscle cells including store-operated calcium entry

One of the principal causes of airway narrowing in asthma is the contraction of smooth muscle cells lining the conducting airways. This contraction is regulated by changes in intracellular calcium concentration ($[Ca^{2+}]_i$). The mechanism controlling $[Ca^{2+}]_i$ primarily involves agonist-induced release of calcium from internal stores. Appropriate refilling of these stores is achieved via calcium influx from the extracellular medium into the cytoplasm, which is then pumped back into the stores by sarcoplasmic/endoplasmic reticulum calcium APTase (SERCA). However, in contrast to other types of muscle cells, calcium influx in airway smooth muscle cells (ASMC) occurs mainly through non-voltage-dependent pathways. In particular, store-operated calcium entry (SOCE), in which calcium influx is triggered by store depletion, has been shown to play an important role. Therefore, in order to account for the characterics of calcium influx observed in human ASMC subject to SERCA block or agonist stimulation [1,2], we develop a mathematical model of calcium dynamics in ASMC that includes SOCE. Preliminary simulations and phase-plane analysis of the model indicate that either direct SOCE into the internal stores, in addition to cytosolic SOCE, or desensitization of cytosolic SOCE by $[Ca^{2+}]_i$, is required to account for the experimental responses reported in [1,2].

This modelling work is part of a larger project aiming at developing a multiscale model of airway hyper-responsiveness in asthma, from the molecular mechanisms of airway contraction at the cellular level to the biomechanics of the whole tissue [3,4].

References

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