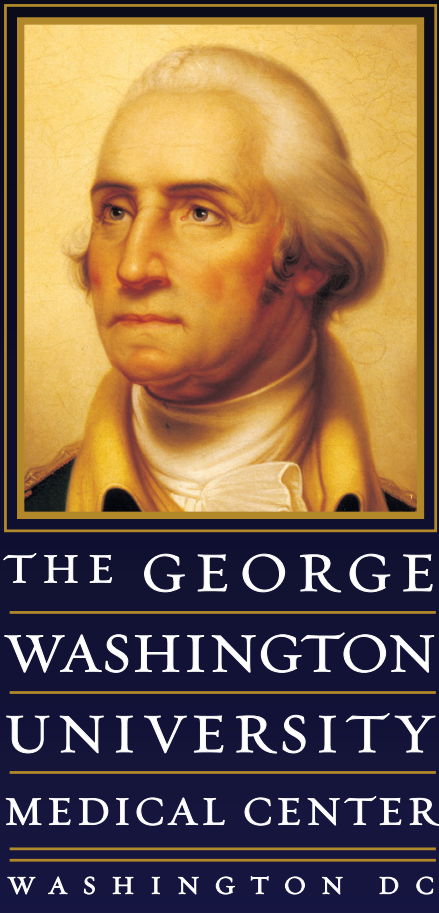




The Effects Of Corticosteroids On NF-KB In Sinonasal Polyposis.

A Preliminary Immunohistochemical Investigation.

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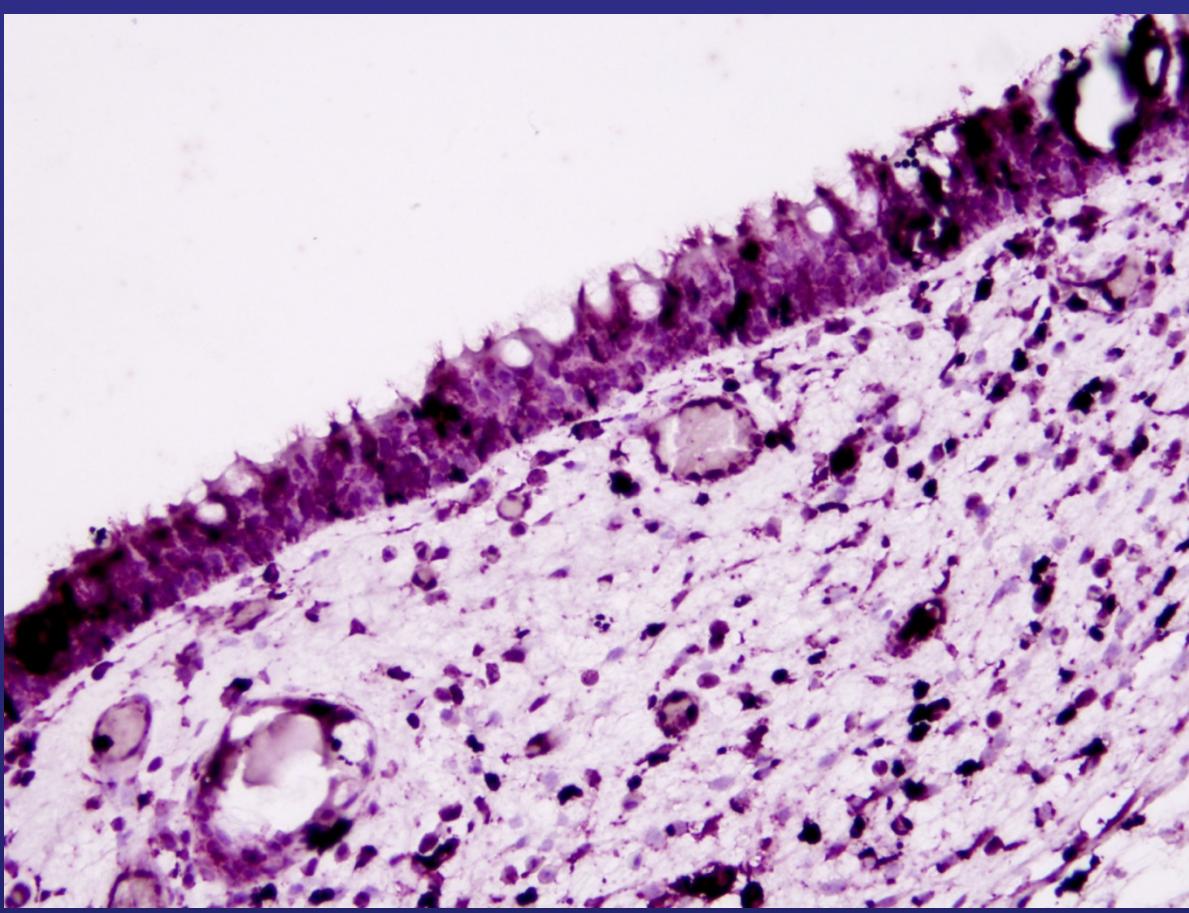


INTRODUCTION

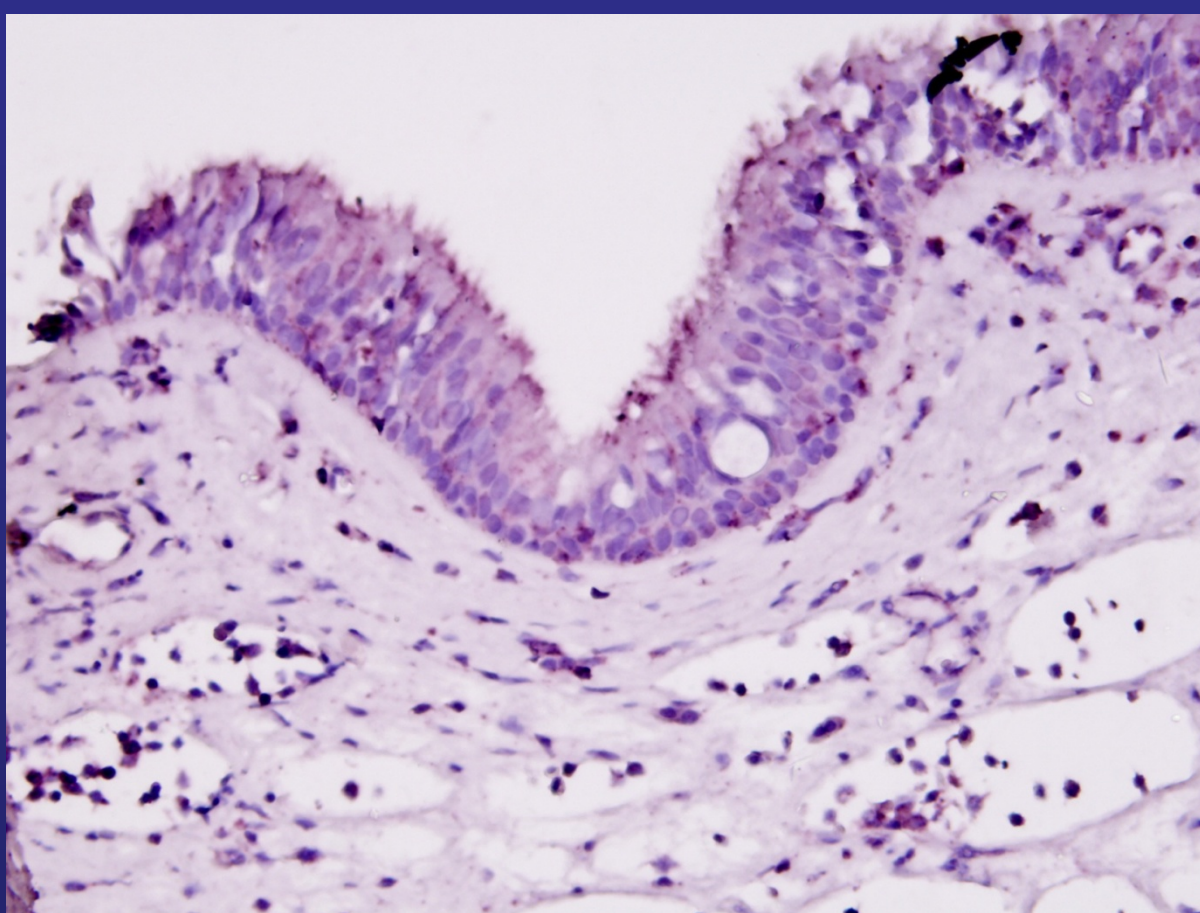
- Nuclear factor kappa B (NF-KB) is a prominent transcription factor involved in the production inflammatory cytokines, and has been shown to play an important role in the etiology of asthma and nasal polyps through augmentation of the inflammatory response and recruitment of eosinophils.
- Steroids have been shown to prevent NF-KB mediated gene expression in three distinct ways (Figure 1). These effects include stabilization of a NF-KB precursor molecule, prevention of nuclear translocation of NF-KB, and inhibition of a specific NF-KB-related transcription factor known as RelA.
- These actions all act to prevent the creation of more inflammatory cytokines, such as TNF-alpha which has been implicated in pathogenesis of polyposis.
- The long-term use of oral corticosteroids however, is hindered by systemic side effects
- We seek to understand the effects of oral corticosteroids on NF-KB and other related molecules in order to find new targets for the treatment of sinonasal polyposis.

METHODS AND MATERIALS

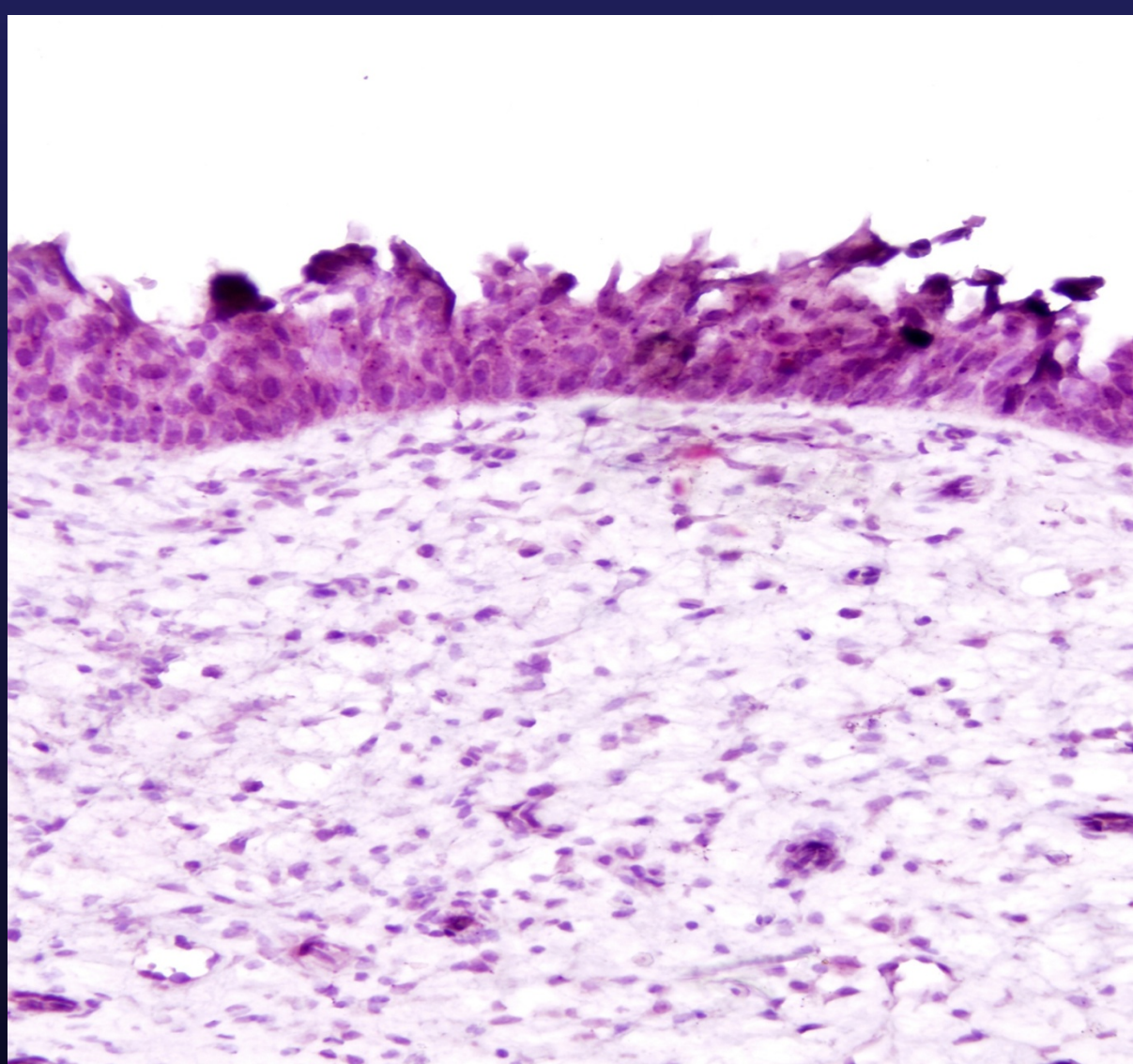
- A non-randomized controlled trial was performed on 10 patients with sinonasal polyposis.
- After meeting study criteria, patients were biopsied, underwent treatment for 6 weeks with an oral corticosteroid regimen, and were re-biopsied.
- Biopsy specimens underwent immunohistochemical staining for NF-KB and Ser32a, an indirect marker of NF-KB activity.
- Sections were analyzed for expression of NF-KB and Ser32a using photometric software.
- Comparisons of gene expression were made before and after corticosteroid treatment.



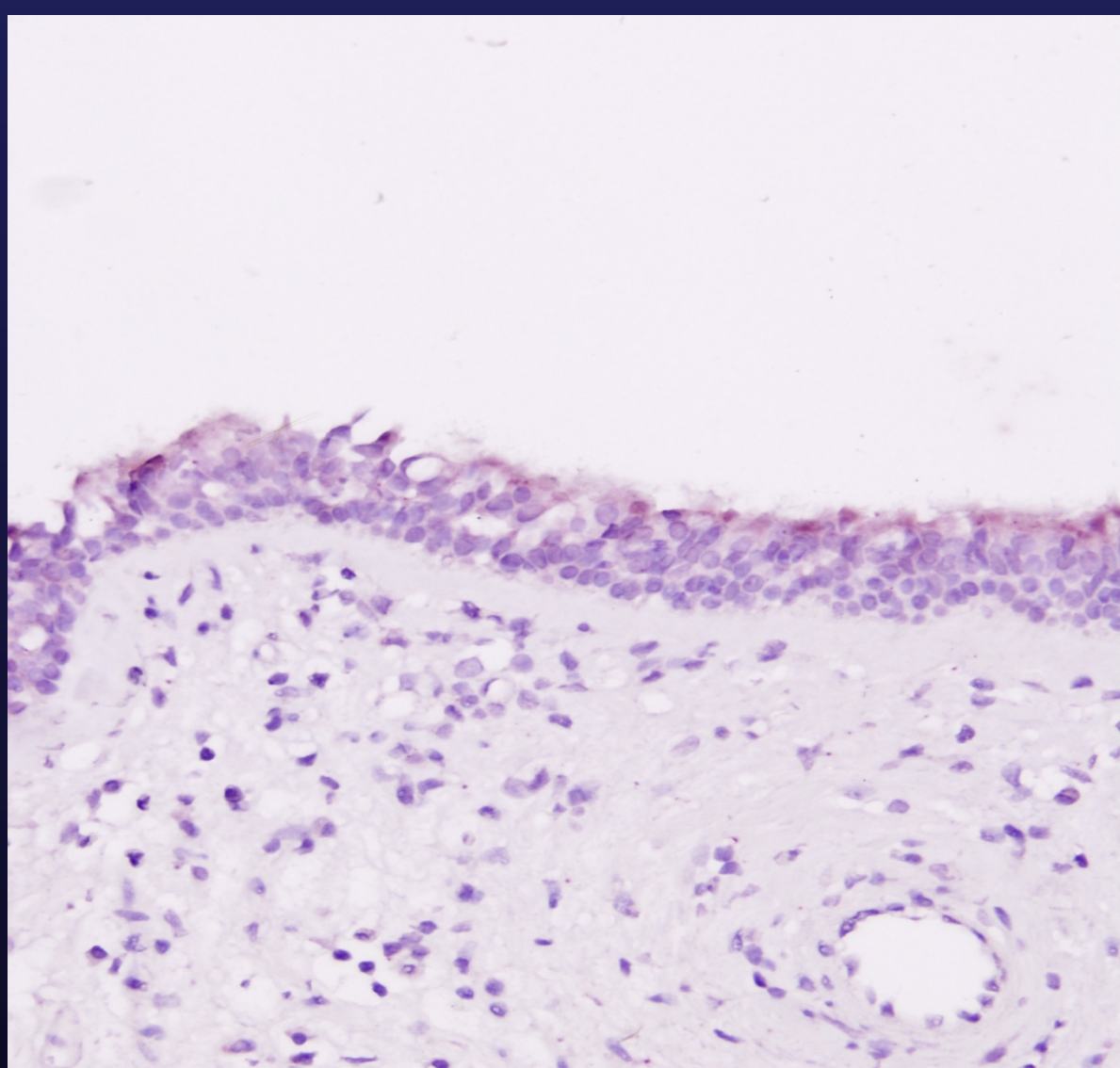
Patient 7, Pre-treatment, NF-KB



Patient 7, Post-treatment, NF-KB



Patient 8, Pre-treatment, Ser 32a



Patient 8, Post-treatment, Ser 32a

RESULTS

- Patient samples were recovered in sufficient quantities for analysis in 4 patients.
- After treatment, the amount of NF-KB positivity was decreased in patients 5, 6, 7, 8 by 35, 32, 65, 78 percent respectively.
- After corticosteroid treatment, Ser32a positivity was decreased by 180, 103, 11, 18% in patients 5, 6, 7, and 8. (Figure 2 and 3)
- The differences between the pre-treatment groups and post-treatment groups were significant (p<0.05).

CONCLUSIONS

- Corticosteroids appear to reduce inflammation in sinonasal polyposis by decreasing levels of NF-KB and related molecules such as Ser32a.
- Studies with larger numbers of patients are necessary to further describe the complex relationships between transcription factors and corticosteroids.
- Quantative studies are required
- This preliminary investigation suggests that NF-KB could be used as a new target molecule in the treatment of sinonasal polyps.
- New drugs can treat nasal polyps more precisely at the molecular level without the adverse side affects of oral steroids.

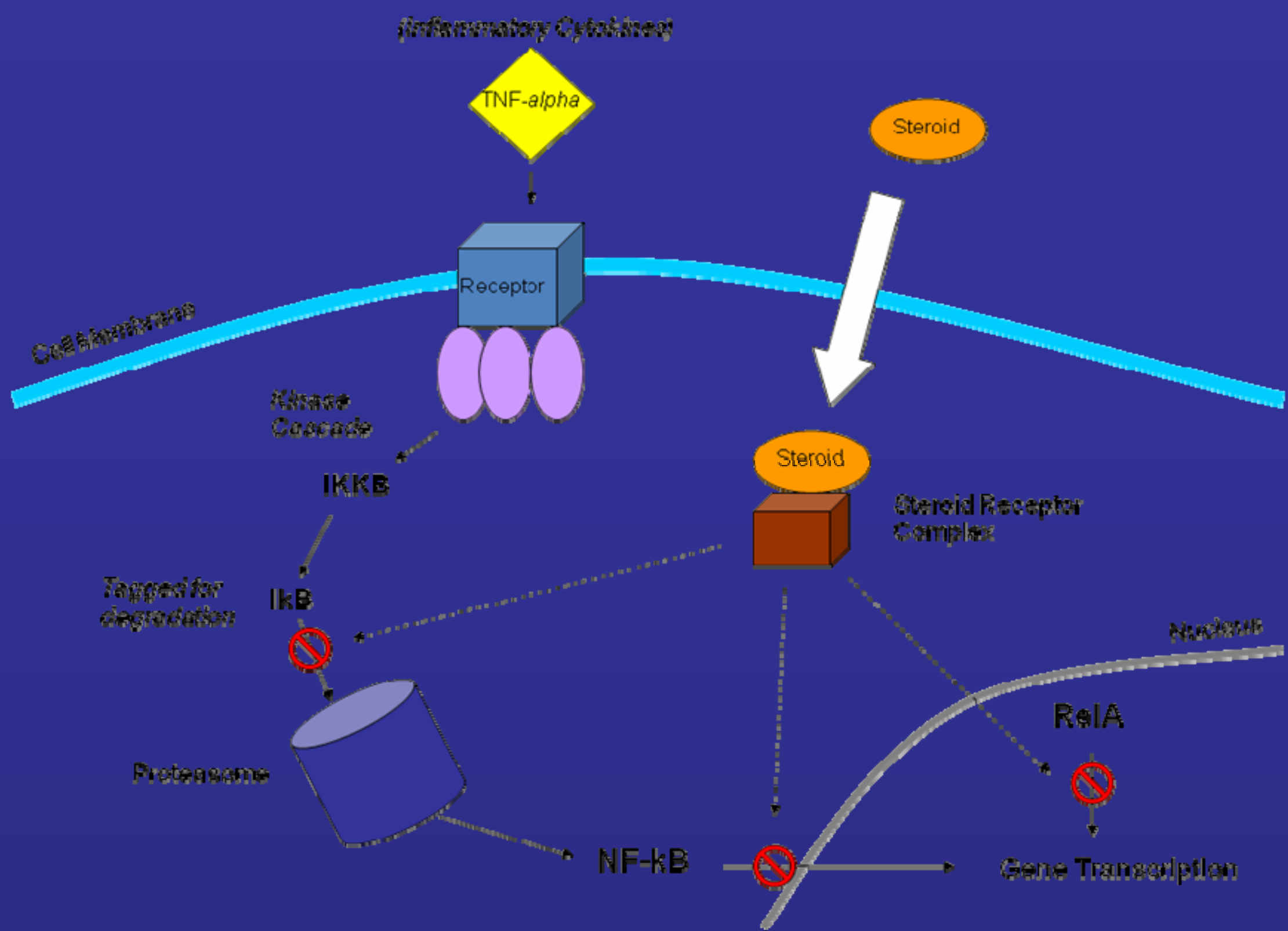


Figure 1. Schematic Representation of NF-KB Action

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