# Evaluation of BRAF and KRAS Gene Expression in Nasal Polyposis

Original Investigation

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Abstract

**Objective:** The goal of this study was to investigate the expression patterns and potential relationship of the Kirsten rat sarcoma viral oncogene homolog (KRAS) and B-raf proto-oncogene (BRAF) genes in nasal polyposis (NP).

**Methods:** Twenty-nine patients were included in the study. Small punch biopsies were collected from nasal polyps during each operation and immediately frozen in liquid nitrogen. Punch biopsies were also taken during surgery from the inferior turbinate or the septum mucosa of the patients as a control group, and these samples were also frozen. Total ribonucleic acid (RNA) was isolated using TRIzol reagent. The gene expression analyses of the KRAS and BRAF genes were performed by the real-time polymerase chain reaction method.

**Results:** When compared to control subjects, KRAS nasal polyp gene expression increased in 21, but decreased in eight of the 29 patients. This statistical analysis revealed a statistically significant difference between the nasal polyp group and the controls (p=0.023). Like KRAS, a decrease was observed in BRAF gene expression in six, and an increase in 23 patients (p=0.011).

**Conclusion:** Our findings suggest a potential association between BRAF and KRAS genes expression and NP, but further studies are needed to confirm this relationship. This finding suggests that the genetic background of NP could be a contributing factor, with the BRAF and KRAS mutations playing a role.

**Keywords:** Nasal polyposis, gene expression regulation, KRAS gene, BRAF gene, mutation, polymerase chain reaction, nasal mucosa, biopsy

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## Introduction

Nasal polyposis (NP) is a common, long-term inflammatory condition affecting the sinus and the nasal mucosa. Characterized by widespread semi-transparent, soft, grape-like abnormal mucosal formations of unknown etiology, it can be easily recognized via endoscopic nasal examination (1-3). Nasal polyps are common in the ethmoid sinuses, the middle turbinates, and the meatus. Although NP is a benign disease with a tendency to recur at varying time intervals in each patient, it is a very disturbing

disease with complaints of nasal obstruction, rhinorrhea, postnasal dripping, and smell loss (1). Deformation of intranasal structures and nasal bones can also be detected in long-term, untreated patients with advanced disease. In NP, while predominant Th2-type inflammation is the characteristic feature of the disease that causes eosinophil-dominated inflammatory cells in polyps, the involvement of numerous molecular markers, cytokines, and chemokine molecules in the disease process make it a very heterogeneous complex inflammatory disease (1-3). The central hypothesis of our study was that the expression levels of the B-raf proto-oncogene (BRAF) and Kirsten rat sarcoma viral oncogene homolog (KRAS) genes are significantly altered in the nasal polyp tissue compared to non-polypoidal nasal mucosa (inferior turbinate or nasal septum mucosa) from the same individuals, suggesting a potential role for these genes in the pathogenesis of NP.

The BRAF is an intracellular serine/threonine protein kinase that effects epidermal growth factor receptor signaling via the mitogen-activated protein kinase (MAPK) downstream signaling route (4,5). The BRAF gene mutation has been extensively studied in thyroid malignancies because it is the leading papillary thyroid cancer associated with a worse prognosis and aggressive tumor behavior (6). On the other hand, this mutation has also been studied in malignant diseases other than thyroid cancer, including colorectal, ovarian, and melanoma, with a management effort on BRAF-dependent kinase inhibitor therapy (7). Rarely, BRAF oncogene mutations have also been studied in non-malignant diseases, including NP and Hashimoto's thyroiditis, other than malignant diseases (2,4). KRAS is a member of the Ras family of genes that has an effector role in some signaling cascades regulating gene expression, such as the MAPK pathway (4). KRAS mutation, like BRAF mutation, is commonly found in various malignancies such as those of the pancreas, the colon, the lungs, the uterus, the brain, and the kidneys. However, studies reporting KRAS mutations in non-malignant diseases that were primarily NP are very rare in the literature (1-3). The goal of the presented study was to investigate the relationship between the NP disease and the gene expression of BRAF and KRAS by comparing the BRAF and KRAS gene expression levels of NP specimens, and the nasal septum or the inferior turbinate mucosa specimens as controls, in the same patients using real-time polymerase chain reaction (PCR) techniques. To the best of our knowledge, this is the first study assessing both BRAF and KRAS gene expression by using real-time PCR in human NP disease.

## Methods

### Patients

This prospective study was conducted in a tertiary university hospital, İstanbul Medeniyet University Göztepe Prof. Dr. Süleyman Yalçın City Hospital, Department of Otorhinolaryngology- Head and Neck Surgery. The study was approved by the Health Sciences İstanbul Medeniyet University Göztepe Training and Research Hospital Clinical Research Ethics Board (approval number: 2017/0083, date: 23.03.2023). All participants provided their informed consent to be included in the study. Initially, 32 patients were included in the study. Three patients were excluded, as two were diagnosed with inverted papilloma and one with antrochoanal polyp after histopathologic examination. The study was conducted with 29 cases who underwent endoscopic endonasal surgery due to NP disease. Of the 29 patients, 19 (65.5%) were male and 10 (34.5%) were female, with ages ranging from 18 to 69 years. Their average age was 44.17±13.76, and the median age was 44 years. The duration of the symptoms ranged from one to 15 years, with an average of 5.21±4.12 and a median time of four years. The number of sinuses treated ranged from 1 to 4 (maxillary, ethmoid frontal, and sphenoid sinuses); the average was 2.38±1.29, and the median was two. Only one patient (3.4%) was a smoker. The exclusion criteria were a medical history of head and neck malignancy with or without head and neck radiation therapy, history of chemotherapy due to malignancy, and age younger than 18 years. Patients aged ≥18 years, had proven NP through rigid or flexible endoscopic endonasal examination, and underwent endoscopic endonasal surgery met our inclusion criteria. All patients had undergone paranasal sinus computed tomography (CT) scan before surgery to predict the extent of the disease and detect altered anatomy due to prior surgery.

### Patients' Clinical Features

There were complaints of nasal obstruction in 96.6% of cases, loss of smell in 27.6%, pain in 13.8%, and asthma in 20.7%. A previous history of endoscopic endonasal surgery for NP was present in 44.8%. Additional chronic diseases, including diabetes mellitus and hypertension, were present in 17.2%, and six (20.7%) had asthma. While 37.3% of the cases had septum deviation, 58.6% did not, and one (4.1%) had a perforated septum due to prior surgery. Hypertrophy in the lower turbinate was present in 55.2%, and 20.7% had middle turbinate findings (Table 1).

### KRAS and BRAF Gene Expression Technique

During the NP procedure, small biopsy specimens were excised, and promptly frozen in liquid nitrogen. In the control group, punch biopsies were collected from the inferior nasal turbinate or the nasal septum mucosa, and the specimens were also subsequently frozen in liquid nitrogen. Total ribonucleic acid (RNA) extractions were conducted utilizing TRIzol reagent. Complementary deoxyribonucleic acids (cDNAs) were synthesized using oligo dT primers with the commercial cDNA synthesis kit. KRAS and BRAF expression studies were conducted via real-time PCR with

particular primers and normalized with the GAPDH gene. The PCR reactions were conducted under the following conditions: initial denaturation at 95 ˚C for 5 minutes, followed by 40 cycles of denaturation at 95 ˚C for 30 seconds, annealing at 60 ˚C for 30 seconds, and extension at 72 ˚C for 30 seconds. The final extension was performed at 72 ˚C for 5 minutes. Each reaction included 2 µL of cDNA template, 1 µL of each primer, 6 µL of nuclease-free water, and 10 µL of SYBR Green master mix in a total volume of 20 µL. Primer pairs are given in Table 2. Expression calculation was done with the 2-CT method.

### Statistical Analysis

Statistical analysis was done using the SPSS 21.0 program with the Wilcoxon signed-rank test, with $p<0.05$ considered as a statistically significant difference. The Wilcoxon signed-rank test revealed statistically significant differences in gene expression for both KRAS ($Z=-2.281$, $p=0.023$) and BRAF ($Z=-2.555$, $p=0.011$). To further support these findings, 95% confidence intervals (CIs) for the median differences were calculated, providing a more robust interpretation of effect size and variability.

## Results

### KRAS and BRAF Gene Expression Results

We found that eight of the 29 samples showed decreased KRAS expression, while 21 showed different rates of increased expression ($p=0.023$). For BRAF, a decrease in expression was observed in six samples, while KRAS expression increased in 23 samples to varying degrees ($p=0.011$). Both BRAF and KRAS gene expression increments were statistically significant ($p<0.05$) (Table 3).

To better interpret the gene expression data presented in Table 3, raw KRAS and BRAF values were normalized by calculating fold changes relative to the median expression level of each gene. Box-plots were used to visualize the distribution and variability of these fold changes (Figure 1). Statistical comparison using the Wilcoxon signed-rank test revealed no significant difference between KRAS and BRAF fold changes ($p=0.151$). However, both Pearson's and Spearman's correlation analyses indicated a strong, statistically significant positive correlation between KRAS and BRAF fold changes (Pearson's $r=0.765$, $p<0.0001$; Spearman's $p=0.789$, $p<0.00001$). These findings suggest that KRAS and BRAF gene expressions tend to increase or decrease in parallel across the patient cohort, implying a potential co-regulatory or pathophysiological link between the two genes in the studied context.

To enhance the robustness of the statistical findings, 95% CIs were calculated for the median differences in gene expression levels. For KRAS, the Wilcoxon signed-rank test yielded a test statistic of 63.0 with a p-value of 0.021, and the 95% CI for the median difference ranged from -0.025 to 0.086. Although statistically significant, the inclusion of zero in the

**Table 1.** Symptoms and clinical findings of nasal polyposis patients included in the study

| Symptoms and findings | | n | % |
|---|---|---|---|
| Nasal obstruction | Yes | 28 | 96.6 |
| | No | 1 | 3.4 |
| Smell loss | Yes | 8 | 27.6 |
| | No | 21 | 72.4 |
| Pain | Yes | 4 | 13.8 |
| | No | 25 | 86.2 |
| Asthma | Yes | 6 | 20.7 |
| | No | 23 | 79.3 |
| Previous FESS surgery | Yes | 13 | 44.8 |
| | No | 16 | 55.2 |
| Additional chronic disease | Yes | 5 | 17.2 |
| | No | 24 | 82.8 |
| Septal deviation | Yes | 11 | 37.9 |
| | No | 17 | 58.6 |
| | Perforated | 1 | 3.4 |
| Inferior turbinate hypertrophy | Yes | 16 | 55.2 |
| | No | 13 | 44.8 |
| Middle turbinate | Not present or partially present | 7 | 24.1 |
| | Present | 22 | 75.9 |

n: Number of patient numbers, FESS: Functional endoscopic sinus surgery

**Table 2.** Primer sequences used for gene expression analysis. PCR conditions-including annealing temperature, cycle number, and reagent concentrations-should be provided to enhance reproducibility

| | |
|---|---|
| GAPDH | F-5'-GGGTGATGCTGGTGCTGAGTATGT-3' |
| | R-5'-AAGAATGGGAGTTGCTGTTGAAGTC-3' |
| KRAS | F-5'-TCTTGCCTCCCTACCTTCCACAT-3' |
| | R-5'-CTGTCAGATTCTCTTGAGCCCTG-3' |
| BRAF | F-5'-GGCAGAGTGCCTCAAAAAGAA-3' |
| | R-5'-AACCAGCCCGATTCAAGGA-3' |

GAPDH: Glyceraldehyde-3-phosphate dehydrogenase, KRAS: Kirsten rat sarcoma viral oncogene homolog, BRAF: B-raf proto-oncogen, PCR: polymerase chain reaction

**Table 3.** BRAF and KRAS gene expression results

| Patients | KRAS results | BRAF results |
|---|---|---|
| 1 | 1.097179246 | 1.175361666 |
| 2 | 1.001621713 | 1.030369095 |
| 3 | 1.018120367 | 1.077038148 |
| 5 | 0.967776972 | 1.017288726 |
| 7 | 0.970051343 | 1.045043215 |
| 8 | 1.128866204 | 1.195048732 |
| 9 | 1.085551034 | 1.074484002 |
| 10 | 0.96099251 | 0.969552211 |
| 11 | 1.088569584 | 1.15297407 |
| 12 | 0.975080824 | 1.083389811 |
| 14 | 0.947106598 | 0.943466947 |
| 15 | 1.080471593 | 1.062976901 |
| 16 | 1.048824264 | 1.014898646 |
| 18 | 0.983468754 | 0.90912133 |
| 19 | 0.971429611 | 0.98634447 |
| 20 | 0.969725294 | 0.95497642 |
| 21 | 1.1043126 | 1.22840006 |
| 22 | 1.124316883 | 1.178283147 |
| 23 | 1.219108282 | 1.270550481 |
| 24 | 1.189088232 | 1.779561132 |
| 25 | 1.03379119 | 1.04301161 |
| 27 | 1.048202537 | 0.941551158 |
| 29 | 1.005388311 | 1.002334551 |

KRAS: Kirsten rat sarcoma viral oncogene homolog, BRAF: B-raf proto-oncogene

CI suggests a relatively modest effect size. In contrast, BRAF expression showed a test statistic of 53.0 with a p-value of 0.008, and the corresponding 95% CI ranged from 0.002 to 0.083. The entirely positive interval for BRAF supports a more consistent and meaningful increase in gene expression. These results strengthen the evidence for altered expression of both KRAS and BRAF in NP, with BRAF demonstrating a potentially stronger association.

## Discussion

While NP is a benign disease that does not show malignant transformation, its symptoms, such as nasal obstruction, smell dysfunction, anosmia, and nasal discharge, can disrupt the comfort and quality of life of patients. One of the most challenging aspects of this disease is its tendency to recur despite surgical intervention, and NP shows recurrences at different time intervals that vary in each patient. Although the etiology of the disease is still unclear, the data obtained from the studies show that genetic and environmental factors have a significant effect on the formation of NP (1-3).

Although our study identifies significant changes in BRAF and KRAS gene expression in NP, the precise functional and mechanistic implications of these alterations were not directly investigated. Recent studies shed light on the potential mechanistic roles of these genes in NP pathology. For instance, a recent investigation demonstrated that the activation of the RAS/RAF/MEK/ERK signaling pathway in nasal polyps contributes significantly to the cell proliferation, inflammation, and tissue remodeling characteristics of NP, suggesting that BRAF and KRAS over-expression could exacerbate these processes (8). Furthermore, integrated genomic analyses combining genome-wide association studies and expression quantitative trait loci have highlighted the involvement of multiple genetic loci, including those related to inflammatory pathways and cellular growth, in the development of NP (9). These findings provide a robust foundation for future functional studies aimed at elucidating the specific roles of BRAF and KRAS gene expression in NP pathology.

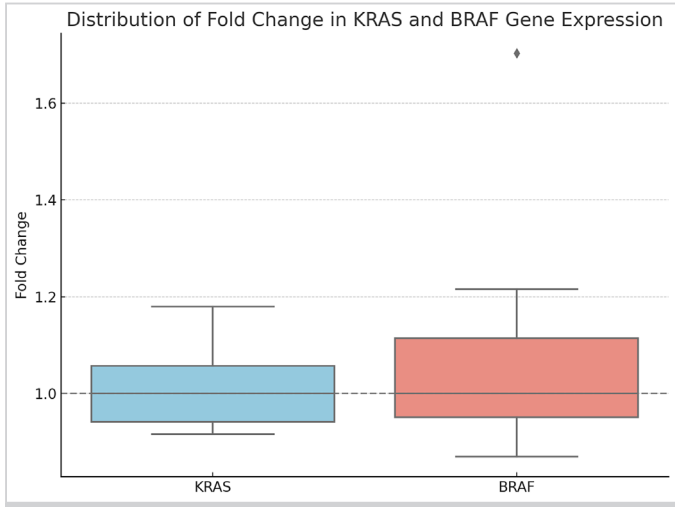


**Figure 1.** Distribution of fold change in KRAS and BRAF gene expression

KRAS: Kirsten rat sarcoma viral oncogene homolog, BRAF: B-raf proto-oncogene

These molecular alterations may account for the chronicity, recurrence tendency, and resistance to treatment seen in some NP patients, although more longitudinal studies are needed to confirm this.

In short, while our findings do not yet translate into immediate clinical decisions, they support the concept that KRAS and BRAF expression changes may eventually serve as molecular markers for disease severity or treatment resistance in NP. This area holds potential for future therapeutic targeting, especially as MAPK pathway inhibitors are well-characterized in other contexts.

The influence of genetic factors and heredity on the occurrence of NP has been well documented in studies showing that the disease was more common in family members and twins (1,10,11). A multi-centric study with

224 patients found a family history rate as high as 52.66% (10). Additionally, a family history of NP was found as 14% in a smaller group of 50 patients (11). A striking finding in the referred study was the presence of NP in more than one family member in 6% of the patients (11). These results indicate that genetic factors may be contributing to NP occurrence, at least in some cases, associated with possible environmental factors.

The impetus of this study was to determine whether NP has a genetic basis, by performing BRAF and KRAS gene expression via the reverse transcription-PCR (RT-PCR) technique. The detection of these genetic mutations is also likely to be a beacon of hope for possible inhibitory therapy for patients with these mutations. We performed gene expression of BRAF and KRAS genes via the RT-PCR technique, comparing immediately fresh-frozen with liquid nitrogen biopsy samples of NP tissue and control tissue samples from inferior turbinate or nasal septum mucosa in the same patient. Similar to NP, a high incidence of KRAS mutation has also been observed in non-neoplastic hyperplastic colon polyps that did not cause malignant transformation (12). KRAS mutation seems to be related to the pathogenesis of NP. We found that KRAS expression and BRAF expression increased in 21 cases and 23 cases out of 29 cases, respectively, and both increases were statistically significant ($p<0.05$). Lin et al. (13) concluded that tumor necrosis factor alpha stimulates chemokine ligand 2 (CCL2) transcription in NP fibroblasts. The B-Raf/MEK/ERK signaling cascade is in charge of CCL2 expression, which is the key factor for the monocyte chemotaxis modulator in NP fibroblasts, leading to macrophage recruitment in the pathogenesis of NP.

In our study, we also found that BRAF was associated with NP pathogenesis, and BRAF expression was increased in NP tissue compared to normal inferior turbinate or septal mucosal tissue. On the other hand, previous research has reported conflicting results regarding BRAF gene expression in NP. For instance, Zaravinos et al. (3) observed decreased levels of BRAF mRNA in NP tissues compared to adjacent turbinate mucosa, contrasting with our findings of increased BRAF expression. These discrepancies could be attributed to methodological variations, differences in patient populations, tissue sampling techniques, or heterogeneity within NP pathology itself. Variations in inflammatory profiles, presence or absence of comorbid conditions such as asthma or allergy, and differences in prior medication usage (e.g., corticosteroids) could also explain these inconsistencies. Given the scarcity of studies investigating BRAF gene expression in NP, it remains difficult to fully elucidate the underlying mechanisms. Therefore, future research should standardize patient selection criteria and methodological approaches to clarify the role of BRAF expression more accurately in NP.

However, studies regarding BRAF and KRAS mutations in NP in the literature are not presently adequate to clarify their part in the pathogenesis of the disease. On the other hand, the MEK1/2-ERK1/2 pathway, which is closely related to these mutations in NP, is activated (phosphorylated) to lead to NP formation, and research in this area is of great interest to a highly active research community (14-16). Much more genes other than BRAF and KRAS have been detected in NP with micro-assay techniques (1). Hyper- and hypo-methylation of some genes, suppression, and increment of gene expression have been found to be closely related to NP (17,18). These findings showed that the complexity of the disease and NP formation is multifactorial, which includes hereditary, epigenetic, environmental, and individual factors interacting with each other.

Our research has certain limitations. It was conducted with a relatively small sample size of 29 patients, which may limit the statistical power and generalizability of the findings. Therefore, it remains unclear whether the sample size was sufficient to detect clinically meaningful differences in KRAS and BRAF gene expression. Future studies are needed with large samples of cases. The other limitation is that the study did not include or control for potentially influential factors such as allergy, asthma, atopy, prior corticosteroid use, or detailed history of smoking, all of which may affect NP pathology and gene expression outcomes. Future research should consider collecting comprehensive data on these factors and adjusting for them in statistical analyses to enhance the validity and interpretability of findings.

## Conclusion

In conclusion, our study identified significant associations between increased BRAF and KRAS expression and the presence of NP, suggesting a potential genetic component to this chronic inflammatory disease. However, these results are correlative and do not establish direct causation. Further experimental studies investigating the causal mechanisms and functional implications of BRAF and KRAS gene expression changes are necessary to clarify their exact roles in NP pathogenesis.

### Ethics

**Ethics Committee Approval:** The study was approved by the Health Sciences İstanbul Medeniyet University Göztepe Training and Research Hospital Clinical Research Ethics Board (approval number: 2017/0083, date: 23.03.2023).

**Informed Consent:** All participants provided their informed consent to be included in the study.

**Footnotes**

**Authorship Contributions**

Surgical and Medical Practices: G.Ö.A., T.Ç., Concept: G.Ö.A., F.Ö., H.İ.Y., O.İ.Ö., T.Ç., Design: G.Ö.A., F.Ö., H.İ.Y., O.İ.Ö., T.Ç., Data Collection and/or Processing: G.Ö.A., F.Ö., H.İ.Y., O.İ.Ö., T.Ç., Analysis and/or Interpretation: G.Ö.A., F.Ö., H.İ.Y., O.İ.Ö., T.Ç., Literature Search: G.Ö.A., F.Ö., T.Ç., Writing: G.Ö.A., F.Ö., O.İ.Ö.

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**Main Points**

- Nasal polyposis has multifactorial causes and adverse effects on patient comfort and quality of life due to frequent relapses.
- Underlying mechanisms of the disease are still uncertain.
- Some genetic, environmental and individual factors interact in leading to the disease.
- A strong correlation was identified between BRAF and KRAS, elevated gene expression, and the disease.
- These findings may play a guiding role in understanding the underlying causes of this disease, the cause(s) of which have not been fully revealed.

## References

1. Wang de Y. Significance of susceptible gene expression profiles in nasal polyposis. Clin Exp Otorhinolaryngol. 2008; 1: 177-83. [Crossreff]
2. Zaravinos A, Bizakis J, Soufla G, Sourvinos G, Spandidos DA. Mutations and differential expression of the ras family genes in human nasal polyposis. Int J Oncol. 2007; 31: 1051-9. [Crossreff]
3. Zaravinos A, Bizakis J, Spandidos DA. RKIP and BRAF aberrations in human nasal polyps and the adjacent turbinate mucosae. Cancer Lett. 2008; 18; 264: 288-98. [Crossreff]
4. Ozdamar OI, Acar GO, Ozen F, Zenginkinet T. Assessment of BRAF-V600E, KRAS, NRAS and EGFR mutations in papillary thyroid carcinoma and Hashimoto's thyroiditis. ENT Updates. 2020; 10: 300-5. [Crossreff]
5. Niault TS, Baccarini M. Targets of raf in tumorigenesis. Carcinogenesis. 2010; 31: 1165-74. [Crossreff]
6. Tufano RP, Teixeira GV, Bishop J, Carson KA, Xing M. BRAF mutation in papillary thyroid cancer and its value in tailoring initial treatment: a systematic review and meta-analysis. Medicine (Baltimore). 2012; 91: 274-86. [Crossreff]
7. Yadav V, Chen SH, Yue YG, Buchanan S, Beckmann RP, Peng SB. Co-targeting BRAF and cyclin dependent kinases 4/6 for BRAF mutant cancers. Pharmacol Ther. 2015; 149: 139-49. [Crossreff]
8. Niu Z, Sha J, Zhu D, Meng C. Investigation and characterization of the RAS/RAF/MEK/ERK pathway and other signaling pathways in chronic sinusitis with nasal polyps. Int Arch Allergy Immunol. 2025; 186: 252-63. [Crossreff]
9. Yoshikawa M, Asaba K, Nakayama T. Prioritization of nasal polyp-associated genes by integrating GWAS and eQTL summary data. Front Genet. 2023; 14: 1195213. [Crossreff]
10. Rugina M, Serrano E, Klossek JM, Crampette L, Stoll D, Bebear JP, et al. Epidemiological and clinical aspects of nasal polyposis in France; the ORLI group experience. Rhinology. 2002; 40: 75-9. [Crossreff]
11. Greisner WA 3rd, Settipane GA. Hereditary factor for nasal polyps. Allergy Asthma Proc. 1996; 17: 283-6. [Crossreff]
12. Glarakis IS, Savva S, Spandidos DA. Activation of the ras genes in malignant and premalignant colorectal tumors. Oncol Rep. 1998; 5: 1451-4. [Crossreff]
13. Lin SK, Kok SH, Shun CT, Hong CY, Wang CC, Hsu MC, et al. Tumor necrosis factor-alpha stimulates the expression of C-C chemokine ligand 2 gene in fibroblasts from the human nasal polyp through the pathways of mitogen-activated protein kinase. Am J Rhinol. 2007; 21: 251-5. [Crossreff]
14. Chiarella E, Lombardo N, Lobello N, Aloisio A, Aragona T, Pelaia C, et al. Nasal polyposis: insights in epithelial-mesenchymal transition and differentiation of polyp mesenchymal stem cells. Int J Mol Sci. 2020; 21: 6878. [Crossreff]
15. Linke R, Pries R, Könnecke M, Bruchhage KL, Böscke R, Gebhard M, et al. The MEK1/2-ERK1/2 pathway is activated in chronic rhinosinusitis with nasal polyps. Arch Immunol Ther Exp (Warsz). 2014; 62: 217-29. [Crossreff]
16. Liu X, Wang X, Chen L, Shi Y, Wei Y. Effects of erythromycin on the proliferation and apoptosis of cultured nasal polyp-derived cells and the extracellular signal-regulated kinase (ERK)/mitogen-activated protein kinase (MAPK) signaling pathway. Med Sci Monit. 2018; 24: 8048-55. [Crossreff]
17. Liu T, Sun Y, Bai W. The role of epigenetics in the chronic sinusitis with nasal polyp. Curr Allergy Asthma Rep. 2020; 21: 1. [Crossreff]
18. Kim JY, Kim DK, Yu MS, Cha MJ, Yu SL, Kang J. Role of epigenetics in the pathogenesis of chronic rhinosinusitis with nasal polyps. Mol Med Rep. 2018; 17: 1219-27. [Crossreff]