**Table S1.** General features of the sequencing

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Sample Name | Asthma Status | Sequence count | Feature count | Base pairs | Average GC Content (%) |
| A.1 | Asthma | 45455 | 29358 | 23343 | 36.26 |
| A.2 | Asthma | 90870 | 58808 | 47690 | 36.26 |
| A.3 | Asthma | 87462 | 56505 | 98894 | 36.26 |
| A.4 | Asthma | 87748 | 59068 | 4267 | 35.16 |
| A.5 | Asthma | 64428 | 42873 | 169174 | 36.26 |
| A.6 | Asthma | 78416 | 57546 | 13554 | 36.26 |
| A.7 | Asthma | 76961 | 49243 | 22339 | 35.16 |
| A.8 | Asthma | 148429 | 108737 | 7530 | 34.06 |
| A.9 | Asthma | 45584 | 33204 | 14809 | 34.06 |
| A.10 | Asthma | 102504 | 80030 | 19327 | 35.16 |
| A.11 | Asthma | 74613 | 51693 | 10040 | 34.06 |
| A.12 | Asthma | 67172 | 42032 | 75551 | 36.26 |
| A.13 | Asthma | 127293 | 96896 | 32881 | 36.26 |
| A.14 | Asthma | 100086 | 64099 | 26355 | 35.16 |
| A.15 | Asthma | 46052 | 31131 | 16315 | 36.26 |
| A.16 | Asthma | 85508 | 57581 | 211593 | 36.26 |
| A.17 | Asthma | 89401 | 62130 | 297435 | 35.16 |
| A.18 | Asthma | 66793 | 45043 | 626245 | 36.26 |
| A.19 | Asthma | 47123 | 33082 | 31375 | 35.16 |
| A.20 | Asthma | 55040 | 35644 | 21837 | 36.26 |
| A.21 | Asthma | 73703 | 51740 | 34387 | 35.16 |
| A.22 | Asthma | 63137 | 40877 | 29618 | 36.26 |
| A.23 | Asthma | 71829 | 47513 | 31877 | 34.06 |
| A.24 | Asthma | 58316 | 39363 | 19829 | 34.06 |
| A.25 | Asthma | 93760 | 58617 | 260538 | 31.86 |
| A.26 | Asthma | 75670 | 47676 | 99145 | 36.26 |
| A.27 | Asthma | 78603 | 54266 | 182728 | 31.86 |
| A.28 | Asthma | 84154 | 63343 | 41917 | 34.06 |
| A.29 | Asthma | 64791 | 42202 | 11876065 | 36.26 |
| NA.1 | No\_ Asthma | 101953 | 70714 | 25473739 | 36.26 |
| NA.2 | No\_ Asthma | 93168 | 66806 |  |  |
| NA.3 | No\_ Asthma | 80355 | 50756 | 107930 | 36.26 |
| NA.4 | No\_ Asthma | 45278 | 34512 | 17433707 | 35.16 |
| NA.5 | No\_ Asthma | 37877 | 29571 | 153612 | 36.26 |
| NA.6 | No\_ Asthma | 78019 | 53156 | 47690 | 35.16 |
| NA.7 | No\_ Asthma | 65412 | 41105 | 12048 | 35.16 |
| NA.8 | No\_ Asthma | 84710 | 59705 | 19327 | 36.26 |
| NA.9 | No\_ Asthma | 54997 | 40516 | 30120 | 35.16 |
| NA.10 | No\_ Asthma | 65047 | 41977 | 47188 | 36.26 |
| NA.11 | No\_ Asthma | 66032 | 43790 | 13052 | 35.16 |
| NA.12 | No\_ Asthma | 90779 | 63913 | 40662 | 35.16 |
| NA.13 | No\_ Asthma | 50937 | 35680 | 129516 | 35.16 |
| NA.14 | No\_ Asthma | 76963 | 50861 | 19076 | 36.26 |
| NA.15 | No\_ Asthma | 33014 | 26318 | 5020 | 36.26 |
| NA.16 | No\_ Asthma | 54929 | 37598 | 28363 | 34.06 |
| NA.17 | No\_ Asthma | 44082 | 31500 | 16566 | 35.71 |
| NA.18 | No\_ Asthma | 81430 | 55668 | 83081 | 31.86 |
| NA.19 | No\_ Asthma | 51003 | 38811 | 123492 | 36.26 |
| NA.20 | No\_ Asthma | 85398 | 57945 | 40913 | 31.86 |
| NA.21 | No\_ Asthma | 41644 | 29918 | 9789 | 35.16 |
| NA.22 | No\_ Asthma | 139105 | 97242 | 57479 | 35.16 |
| NA.23 | No\_ Asthma | 82084 | 54553 | 337595 | 35.16 |
| NA.24 | No\_ Asthma | 85448 | 60945 | 663644 | 36.26 |
| NA.25 | No\_ Asthma | 72911 | 53627 | 260036 | 35.16 |
| NA.26 | No\_ Asthma | 51271 | 37446 | 13554 | 36.26 |
| NA.27 | No\_ Asthma | 87133 | 58200 | 13303 | 35.16 |
| NA.28 | No\_ Asthma | 58217 | 39985 | 69025 | 36.26 |

**Table S2.** P values based on Wilcoxon signed-rank test for Observed and Shannon index differences among asthmatics and non-asthmatics

|  |  |  |
| --- | --- | --- |
| Observed | | |
|  | Non\_Asthma | Asthma |
| Non\_Asthma | NA | 0.144 |
| Asthma | 0.144 | NA |
| Shannon | | |
|  | Non\_Asthma | Asthma |
| Non\_Asthma | NA | 0.145 |
| Asthma | 0.145 | NA |

**Table S3.** Predicted pathways and relationship with asthma and allergies.

|  |  |  |
| --- | --- | --- |
| Reference | Pathway | Major Findings |
| Joyce and Gahan, 2017 | Secondary bile acid biosynthesis | “Extraintestinal diseases and syndromes such as asthma and obesity may be linked to aberrant bile acid profiles in the host” |
| Zhao et al., 2001 | Penicillin and cephalosporin biosynthesis | “IgE antibodies in the sera of subjects allergic to beta-lactam antibiotics detect a spectrum of specificities ranging from side-chain groups to an entire penicillin or cephalosporin molecule” |
| Rodriguez-Perez et al., 2017 | Fatty acids biosynthesis | “Fatty acids and lipid mediator signaling play an important role in the pathogenesis of asthma, yet this area remains largely underexplored” |
| Cho et al., 2004 | Lipoic acid metabolism | “alpha-Lipoic acid inhibits airway inflammation and hyperresponsiveness in a mouse model of asthma” |
| Revyakina et al., 2019 | Riboflavin metabolism | “The results indicate a decrease in the concentration of magnesium and normal levels of vitamin B2 in serum in patients with bronchial asthma and obesity” |
| Ho et al., 2012 | Galactose metabolism | “These metabolite changes suggest alterations of energy metabolism in asthmatic lungs, with (…) reductions in carbohydrates, such as (…) galactose” |
| Kowal et al., 2019 | Sphingolipid metabolism | “Altered sphingolipid metabolism is associated with asthma phenotype in house dust mite-allergic patients” |
| Liu et al., 2018 | Glyoxylate and dicarboxylate metabolism | "Pathway topology enrichment analysis revealed that (…) glyoxylate and dicarboxylate metabolism (…) pathway in serum are suggested to be significant pathways related to obese asthma” |
| Payne and Freishtat, 2012 | Steroid hormones biosynthesis | “Steroid hormones (eg, glucocorticoids) are ubiquitous in the short-term and long-term management of all types of asthma” |
| Yu et al., 2016 | Purine metabolism | “Purine metabolism was the most prominently influenced in OVA-induced asthma mice according to the metabolic pathway analysis (MetPA), suggesting that significant changes in inflammatory responses in the pathophysiologic process of asthma” |