Table 1. Autism-Associated Homeobox Domain Genes with Functional Roles in Brain Development

| **Gene ID** | **Gene Name** | **GIFtS** |
| --- | --- | --- |
| *ZEB1* | Zinc Finger E-Box Binding Homeobox 1 | 56 |
| *PBX1* | PBX Homeobox 1 | 55 |
| *NKX2-1* | NK2 Homeobox 1 | 54 |
| *ZEB2* | Zinc Finger E-Box Binding Homeobox 2 | 54 |
| *OTX2* | Orthodenticle Homeobox 2 | 53 |
| *NKX2-5* | NK2 Homeobox 5 | 52 |
| *SATB2* | SATB Homeobox 2 | 52 |
| *CUX1* | Cut Like Homeobox 1 | 52 |
| *EMX2* | Empty Spiracles Homeobox 2 | 51 |
| *ARX* | Aristaless Related Homeobox | 50 |
| *SIX3* | SIX Homeobox 3 | 50 |
| *ADNP* | Activity-Dependent Neuroprotector Homeobox | 50 |
| *DLX5* | Distal-Less Homeobox 5 | 50 |
| *LMX1B* | LIM Homeobox Transcription Factor 1 Beta | 50 |

Data curated from GeneCards. **GIFts**: GeneCards Inferred Functionality Score

Table 2. Pharmacological Treatment and Management of Autism Spectrum Disorders

| **Drug Class** | **Mechanism of Action** | **Clinical Applications in Pediatric Disorders** | **Targeted Behavioral Indices** | **Individual Side Effects** |
| --- | --- | --- | --- | --- |
| Risperidone    (Atypical Antipsychotic) | D2, 5HT2A Receptor Antagonist | ASD | Behavioral Irritability, Stereotyped Behaviors | **↑** Appetite, Weight Gain |
| Aripiprazole    (Atypical Antipsychotic) | Partial D2 Receptor Antagonist. Partial 5HT1A Receptor Agonist | ASD | Behavioral Irritability | **↑** Appetite, Weight Gain |
| Haloperidol    (Typical Antipsychotic) | D2 Receptor Antagonist | ASD | Behavioral Hyperactivity | **↑** Extrapyramidal Symptoms (Dystonia) |
| Sertraline    (Antidepressant and Antianxiety) | 5HT Reuptake Inhibitor | ASD with Fragile X Syndrome | Lexical and Semantic Indices | **↑↓** Restlessness and Hyperactivity |
| Methylphenidate    (Psychoactive) | NE and DA Reuptake Inhibitors | ASD with ADHD | Hyperactivity and Attention Deficits | **↓** Appetite, Abdominal Pain, Insomnia |

Autism Spectrum Disorders can be managed with appropriate pharmacotherapy. Selective dopamine (DA) and serotonin (5HT) based-drugs are the mainstay of pharmacological treatment [72,73]. Additional neurotransmitter systems (e.g., norepinephrine (NE) and histamine) are also drug targets. It is not known whether the listed drugs regulate epigenetic mechanisms to counteract autistic symptoms. What is broadly known is that atypical, typical and psychoactive drugs act on DA and 5HT signaling pathways within regions of the human brain (e.g., cortex and basal ganglia) that are behaviorally relevant to the pathophysiology of ASD. Attention Deficit Hyperactivity Disorder (ADHD) and Fragile X Syndrome are debilitating psychiatric conditions commonly diagnosed in pediatric populations. Fragile X Syndrome is a monogenic inherited disease leading to cognitive disability and ASD. Another psychiatric disorder with social deficits and stereotyped behaviors similar to those of autism is Angelman Syndrome (AS). Loss of activity of the maternally inherited *UBE3A* gene causes AS. This particular imprinted gene codes for an E3-ubiquitin ligase which is critical for synaptogenesis throughout brain development [74]. Altogether, these clinical observations suggest that ADHD, Fragile X Syndrome and AS share several epigenetic and phenotypic features with ASD.

Table 3. Examples of Antigen Combinations Associated with MAR ASD

| **Example of antigen combination** | **% found in mothers of children with ASD** | **% found in mothers of typically developing children** |
| --- | --- | --- |
| LDH + YBX1 | 2% | 0% |
| YBX1 + CRMP2 | 5% | 0.6% |
| LDH + GDA + STIP1 | 5% | 0.6% |
| LDH + CRMP1 + STIP1 | 5% | 0% |
| STIP1 + CRMP1 + GDA | 7% | 0.6% |
| LDH + CRMP1 + STIP1 + GDA | 2% | 0% |