

Table S1: All 37 Molecular Autism Publications from Africa (2016–2022).

Authors	Year	Title	Cohort	Cohort phenotyping	Method	Main result
El-Baz <i>et al.</i>	2016	Chromosomal abnormalities and autism.	30 ASD (2-9 yrs; 23M,7F).	DSM-IV-TR ; Stanford-Binet IQ scale and CARS. Clinical examination, neurological examination, EEG and audiological assessment.	High resolution karyotyping.	No detectable numerical or structural chromosomal abnormalities.
Khaled <i>et al.</i>	2016	Altered urinary porphyrins and mercury exposure as biomarkers for autism severity in Egyptian children with autism spectrum disorder.	40 ASD, 40 unrelated controls (3-6 yrs; 20M, 20F) and 20 typically developing siblings of the ASD children (3-15 yrs).	DSM-IV-TR, ADI-R, and CARS.	Urinary (high-performance liquid chromatography (HPLC) with MS/MS (Tandem mass) spectrometry) & blood (cold vapor atomic absorption spectrometry) analysis.	Children with ASD had significantly higher levels of urinary Hg, Pb, and the porphyrins pentacarboxyporphyrin, coproporphyrin, precoproporphyrin, uroporphyrins, and hexacarboxyporphyrin. A significant positive correlation between the levels of coproporphyrin and precoproporphyrin and autism severity; ASD children also had increased blood Hg and Pb levels.
Khemir <i>et al.</i>	2016	Autism in Phenylketonuria Patients: From Clinical Presentation to Molecular Defects.	15 Tunisian and 4 Algerian phenylketonuria patients (2-15 yrs; 7M, 12F).	CARS and ADI-R.	RT-QPCR amplification and sequencing of 5 exons in the phenylalanine hydroxylase (PAH) gene.	15 patients had ASD; identified 6 mutations; no correlation between autism and mutations affecting the phenylalanine hydroxylase gene.
Desoky <i>et al.</i>	2017	Biochemical assessments of thyroid profile, serum 25-hydroxycholecalciferol and cluster of differentiation 5 expression levels among children with autism.	60 ASD (7+/-2.34 yrs; 55M, 5F) and 40 controls (age 7.91 +/-3.21 yrs; 20M, 20F).	CARS.	Biochemical assays of thyroid function: free triiodothyronine (FT3), free tetraiodothyronine (FT4), thyroid-stimulating hormone (TSH) and 25(OH)D with commercially available enzyme-linked immunosorbent assay (ELISA) kits, while CD5 expression levels were measured using flow cytometry.	Significantly higher mean serum TSH levels & mean CD5 expression levels; significantly lower mean serum 25(OH)D levels in ASD group; negative correlation between CD5 with FT3, FT4 and 25(OH)D. ASD severity correlated negatively with FT3 and 25(OH)D and positively with CD5.
Elserogy <i>et al.</i>	2017	Chromosomal aberrations in children with autism spectrum disorders in Upper Egypt.	231 ASD (3-13 yrs; 132M, 99F).	DSM-V, CARS and Stanford Binet Intelligence Scale.	Karyotyping & Fluorescence in situ hybridization (FISH).	11 patients (4.7%) with chromosomal abnormalities; 5 patients with sex chromosome aneuploidy, including 2 patients with Turner syndrome, 2 with 47XYY and 1 with 47XXY. 3 patients had Down syndrome, 1 patient with monosomy 1p36, 1 patient with Williams-Beuren syndrome and 1 patient with a deletion of the long arm of chromosome 13.

Meguid <i>et al.</i>	2017	Dietary adequacy of Egyptian children with autism spectrum disorder compared to healthy developing children.	80 ASD (4–6 yrs, 40M, 40F) and 80 controls (matched gender, age, and family economic status).	DSM-IV-TR, CARS, ADI-R.	Biochemical analysis of micro- and macronutrient profiles.	No differences in total kilocalories, carbohydrate and fat intake. 23.8% of ASD group vs. 11.3% of controls had a protein intake below the Recommended Dietary Allowance. Children with ASD had low intake of calcium (Ca), magnesium (Mg), iron (Fe), selenium (Se) and sodium (Na), also they had significantly high intake of potassium (K) and vitamin C. Serum Mg, Fe, Ca, folate and vitamin B12 was significantly lower in ASD.
Oshodi <i>et al.</i>	2017	Oxidative stress markers and genetic polymorphisms of glutathione S-transferase T1, M1, and P1 in a subset of children with autism spectrum disorder in Lagos, Nigeria.	42 ASD (4-14 yrs) and 23 age-matched controls.	DSM-V and a clinical interview.	Measurement of blood Superoxide dismutase activity; reduced glutathione (GSH) content; lipid peroxidation; Glutathione S-transferase activity; Genotyping of Glutathione S-transferase polymorphism with single tube multiplex amplification refractory mutation system-polymerase chain reaction (ARMS-PCR).	Reduced glutathione in ASD was significantly lower than the control but other oxidative stress markers were not altered. While frequencies of GSTT1 and GSTM1 null genotypes were lower among the controls, the distribution of GSTT1, GSTM1, and GSTP1 polymorphisms was not associated with autism.
Saad <i>et al.</i>	2017	Frequency of Dendritic Cells and Their Expression of Costimulatory Molecules in Children with Autism Spectrum Disorders.	32 ASD (2.5-5 yrs; 22M,10F) and 30 controls (3-6 yrs; 20M,10F).	DSM-V, structured parent interviews; CARS and Aberrant Behavior Checklist (ABC).	Measurement of myeloid dendritic cells (mDCs) and plasmacytoid dendritic cells (pDCs) and the expression of CD86 and CD80 on the entire DCs were detected by flow cytometry. Serum level of 25-hydroxycholecalciferol (25 (OH)D) was estimated using the 25-OH Vit D ELISA Kit.	ASD children had significantly higher percentages of mDCs and pDCs which correlated inversely with serum 25-hydroxyvitamin D levels.
Arony, Gazda and Kitara.	2018	Could nodding syndrome in Northern Uganda be a form of autism spectrum disorder? an observational study design.	47 NS patients (6-19 yrs; male to female ratio was 1.5:1).	Participants were recruited in accordance with WHO surveillance case definition of probable NS; questionnaire was used to investigate the current and past physiological, psychosocial and mental health	Metabolic analysis on blood and urine.	Biotinidase & Acetyl carnitine deficiency (suggested deficiency in mitochondrial fatty acid metabolism); Low BMI; urate concentration was generally normal (83%); the urate/creatinine ratio was generally low (66%) and the other organic acids were high.

				conditions of NS children.		
El-Baz, Mowafy and Lotfy.	2018	Study of serum copper and ceruloplasmin levels in Egyptian autistic children.	20 ASD (2-13 yrs; 15M, 5F) and 20 controls (4-17 yrs; gender-matched).	ICD-10, CARS and Stanford Binet Intelligence Scale.	Measurement of blood serum copper and ceruloplasmin.	Significant difference between ASD and controls in stereotypic movements, absent eye contact, delayed motor development, delayed speech and IQ. Mean level of copper and ceruloplasmin was significantly higher in ASD.
Fagbayi <i>et al.</i>	2018	Neurotransmitter and amino acid levels in Nigerian children with autism spectrum disorders.	18 ASD (8.44±4.87 yrs) and 13 age and gender-matched controls (8.15±4.88yrs).	DSM-IV-TR.	Reversed-phase high performance liquid chromatography (RPHPLC) to measure plasma levels of 20 amino acids (AA) (including neurotransmitters-GABA and glutamate).	Plasma levels of glutamate, glutamine, GABA, tryptophan and cysteine were significantly altered in ASD.
Grayaa <i>et al.</i>	2018	Plasma oxysterol profiling in children reveals 24-hydroxycholesterol as a potential marker for Autism Spectrum Disorders.	36 ASD (36-84 months; 23M, 13F) and 38 age- and gender-matched controls.	DSM-V and CARS.	Standard lipid profile (total cholesterol, triglycerides, and high-density lipoprotein-cholesterol), serum glucose, high-sensitive C-reactive protein and orosomucoid levels were measured utilizing standard techniques. Oxysterol levels were measured by isotope-dilution gas chromatography/mass spectrometry.	Children with ASD had higher plasma 24-hydroxycholesterol, which was inversely correlated with age. Borderline significance was observed for 7 α -hydroxycholesterol, and 25-hydroxycholesterol.
Hamzawy <i>et al.</i>	2018	Leptin and camel milk abate oxidative stress status, genotoxicity induced in valproic acid rat model of autism.	Valproic acid rat model; 10 VPA and 10 controls each containing untreated, camel milk and leptin subgroups.	Autistic behaviours of male offspring were checked by preliminary behaviour tests, including grooming test and elevated pulz maze test.	Kit-based measurement of TNF- α , IL-1 β and IL-6 , GPx, MDA, SOD, dopamine and serotonin and RT-QPCR to measure expression of tumor necrosis factor (TNF)- α , Bax and caspase-3.	VPA altered oxidative stress markers, neurotransmitters and inflammatory cytokines. Significantly increased serum TNF- α , IL-1 β and IL-6 , significantly increased MDA in brain tissue and decreased activity of SOD, GPx and catalase. Significant increase of dopamine and decrease of serotonin. Increased expression of tumour necrosis factor (TNF)- α , Bax and caspase-3. Leptin or CAM alone showed no signs of toxicity; both induced significant improvement of all measured parameters with more pronounced effect with CAM.
Meguid <i>et al.</i>	2018	Contribution of chromosomal abnormalities at 10q and 22q to autism.	3 ASD (4-10 yrs; 2M, 1F).	DSM-V, ADI-R, CARS, ADOS and Stanford Binet scale.	Karyotyping; Array comparative hybridization with Cytochip ISCA array (BlueGenome-version 1.0); Fluorescence In-Situ Hybridization (FISH).	3 children with ASD with chromosomal abnormalities at 10q and 22q. Patient one had a terminal deletion of approximately 6.27Mb in size on the long arm (q-arm) of chromosome 22 at chromosomal band 22q13.31 extending to 22q13.33, which overlaps with deletion syndrome (Phelan-McDermid Syndrome). The deleted region contains many RefSeq/OMIM genes including the SHANK3 gene. Patient three had a heterozygous 36.7 Mb duplication at 10q11.23–q23.2, which contained many RefSeq/OMIM genes including EGR2, NRG3 and GRID1.

O'Connell <i>et al.</i>	2018	The genetic architecture of schizophrenia, bipolar disorder, obsessive-compulsive disorder and autism spectrum disorder.	Gene lists were obtained from previously published studies for ASD (number of genes, n = 792), BD (number of genes, n = 291), SCZ (number of genes, n = 560) , and OCD (number of genes, n = 153).	N/A	Gene list enrichment analyses using Enrichr.	10 genes were commonly associated with the etiology of ASD, SCZ, BD and OCD and these were involved in the dopaminergic and serotonergic pathways, the voltage-gated calcium ion channel gene network, folate metabolism, regulation of the hippo signaling pathway, and the regulation of gene silencing and expression.
El Fotoh <i>et al.</i>	2019	Autism Spectrum Disorders: The Association with Inherited Metabolic Disorders and Some Trace Elements. A Retrospective Study.	320 ASD (age of onset 6.77±2.45 yrs; 228M, 92F).	DSM-V and CARS.	Serum ammonia, blood lactate, and arterial blood gases, plasma amino acid profile by tandem mass spectrophotometry, and a urinary organic acid assay; measured serum lead, mercury, copper, and plasma zinc.	Inherited metabolic disorders were identified in 8 (2.5%) patients as follows: 7 (2.19%) with phenylketonuria, and 1 (0.31%) with glutaric aciduria type 1. 16 (5%) patients had low plasma Zn, 5 (1.56%) had high serum Cu, 2 (0.62%) children had high serum Pb and only 1 (0.31%) had high serum Hg. Electroencephalogram (EEG) abnormalities were reported in 13.12% and Magnetic Resonant Imaging (MRI) abnormalities in 8.43% of cases.
Eshra <i>et al.</i>	2019	Omega-3 modulates anxiety and improves autistic like features induced by high fat diet but not valproate.	VPA rat model; VPA and control females each comprising of 6 controls, 6 high fat diet and 6 high fat diet with omega 3 supplementation.	neurodevelopmental assessment and behavioral tests using elevated plus maze and social interaction in open field.	Mitochondrial complex-1 activity, brain H2O2, TAC (total antioxidant capacity) and IL-6 were measured, in addition to relative gene expression of syntaxin1A and FoxO1 gene. Kit-based measurement of GABA, serotonin and NPY.	Elevated plus maze and social interaction tests indicated severe anxiety in both HFD group and Valp group with more improvement in HFD-omega than Valp-omega group. Valp did not alter serum triglycerides, increased brain H2O2, decreased brain complex 1 and TAC and increased brain IL6. VPA also increased brain expression of FOXO1 and decreased syntaxin expression, levels of serotonin and GABA and increased neuropeptide Y. The effects of omega3 mitigated effects induced by high fat diet but not those induced by VPA. Anxiety and social withdrawal was markedly reduced in HFD-Omega but not VPA-Omega group. Omega-3 intake during pregnancy dampened the effect of prenatal intake of HFD either by lowering TGs levels and state of neuroinflammation or by exerting up-regulation of syntaxin1A and modulation of serotonin levels.
Hassan <i>et al.</i>	2019	Possible Metabolic Alterations among Autistic Male Children: Clinical and Biochemical Approaches.	73 ASD (7.13 yrs ± 3.52, 73M, 0 F) and 73 gender-matched controls (7.76 yrs±4.37).	CARS, short sensory profile (SSP) and Stanford-Binet Intelligence Scales.	Serum markers of mitochondrial dysfunction (lactate, pyruvate, and lactate to pyruvate ratio, creatine kinase (CK), L-carnitine, ammonia, lactate dehydrogenase, pyruvate kinase, alanine transaminase and aspartate transaminase) and oxidative stress were	There was evidence of mitochondrial dysfunction among autistic children: plasma levels of lactate and serum pyruvate, lactate/pyruvate ratio, CK, PK, LDH and ammonia were significantly higher in ASD while the levels of serum L-carnitine and urea were significantly lower. Serum total oxidant status was higher while antioxidant capacity was lower, indicative of oxidative stress. Levels of heavy metals in the blood (Hg, Pb, Al) were significantly higher in ASD. Additionally, there were significantly lower serum total cholesterol, cortisol and estradiol as well as significantly higher dehydroepiandrosterone (DHEA) and free testosterone (p < 0.05 for all markers). 28 (38%) cases were positive for H. pylori antigen in their stool with significant

					measured using kit-based ELISAs or colorimetric assays. Serum cholesterol, cortisol, free testosterone, estradiol, dehydroepiandrosterone, adenosine deaminase were similarly measured and blood levels of heavy metals (mercury, lead and aluminum) were measured using atomic absorption spectrophotometry. Helicobacter pylori antigen in stool samples was detected using the rapid one-step H. pylori card test.	higher serum ammonia and lower adenosine deaminase than in H. pylori-negative autistic children. Specific behavioral markers of ASD correlated significantly with serum pyruvate, urea, uric acid and free testosterone, as well as antioxidant capacity.
Irwin <i>et al.</i>	2019	Maternal Gestational Immune Response and Autism Spectrum Disorder Phenotypes at 7 Years of Age in the Seychelles Child Development Study.	788 mother-child pairs from the Seychelles Child Development Study Nutrition Cohort 2. After exclusions, the final overall sample size was 748, with sample sizes ranging from 691 to 702 per analysis due to missing data in inflammatory markers or covariates and ranging from 687 to 697 after outlier removal.	Social Communication Questionnaire (SCQ) and Social Responsiveness Scale (SRS) were administered at age 7 years.	13 inflammatory markers were measured in mothers' serum at 28 weeks' gestation using a Meso Scale Discovery (MSD) multiplex assay. Measured cytokines were used to determine the sum of T-helper 1 (Th1) and 2 (Th2) cytokines.	Increased MCP-1 (a chemokine that is upregulated in response to pro-inflammatory cytokines) was associated with fewer ASD symptoms while Increased IL-4 (a cytokine that is typically associated with an enhanced anti-inflammatory response) was associated with more ASD symptoms. Higher IL-10 levels were associated with fewer ASD symptoms. No other inflammatory marker variables (IL-1 β , IL-2, IFN- γ , TNF- α , IL-5, IL-10, IL-6, TARC, sFlt-1, VEGF-D, CRP, Th1, Th2, Th:Th2) were significantly associated with SRS or SCQ total scores.
Ismail <i>et al.</i>	2019	Study of C677T variant of methylene tetrahydrofolate reductase gene in autistic spectrum disorder Egyptian children.	78 ASD (3-6 yrs; 65M, 13F) and 80 age- and gender-matched controls.	(DSM)-V-R and CARS.	MTHFR genetic variant, rs1801133(C677T) was studied by using polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) methods followed	MTHFR (C677T) allele frequency was higher significantly in ASD. Combined CT + TT genotypes were more distributed among patients with consanguinity and family history of psychological disorder. The severity of the autistic behavior showed no significant association with MTHFR genotypes.

					by Genotyping by Sanger sequencing method.	
Chehbani <i>et al.</i>	2020	The status of chemical elements in the blood plasma of children with autism spectrum disorder in Tunisia: a case-control study.	89 ASD (7.52 ± 3.02 yrs; 74M, 14F) and 70 controls (7.81 ± 3.42 yrs; 41M, 29F).	DSM-V, ADI-R, ADOS-2 and CARS.	The levels of 33 chemical elements were analyzed by inductively coupled plasma spectrometry (ICP-MS).	There were significant differences in the levels of 8 elements between the two groups, among which there were three rare earth elements (REEs): Eu, Pr, and Sc; four heavy metals: Bi, Tl, Ti, and V; and one essential element: Cu. Children with ASD had higher levels of Er, Pr, Sc, Bi, Tl, Ti, and V, and lower levels of Cu. The children exposed to passive smoking had lower levels of lead (Pb). Four elements (Cr, Er, Dy, and Pr) were negatively correlated to the severity of ASD. The level of Cu was significantly associated with autistic children's behavior.
Esmail <i>et al.</i>	2020	The potential impact of COMT gene variants on dopamine regulation and phenotypic traits of ASD patients.	52 children with ASD (38M, 14F, 4–18 yrs).	DSM-5 and CARS.	Exon 4 of the COMT gene was sequenced by direct Sanger Sequencing, and dopamine levels were measured using a kit-based ELISA.	Three COMT variants were found with 9 haplotypes, and these were associated with abnormal dopamine levels and abnormal EEG. The rs4680 V/M was significantly associated with low dopamine level while rs4680 M/M was significantly associated with high levels. The presentation of three SNPs of COMT were correlated with the EEG.
Kamga <i>et al.</i>	2020	Cascade testing for Fragile X syndrome in a rural setting in Cameroon (Sub-Saharan Africa).	46 participants; 23 children (9.4 ± 5 yrs) and 23 adults (45.9 ± 15.9 yrs); 9M, 27F.	neurologic status was evaluated by determining the levels of support they needed to attain an optimal personal functioning based on the DSM-V.	DNA from blood samples was used to sequence CGG repeats; analysis of the disease associated CGG FMR1 repeat region was performed using the AmpliX FMR1 PCR kit and capillary electrophoresis.	Of the 46 participants who underwent Fragile X carrier testing, 28 (60.87%) were normal (CGG repeats < 55); among them, the CGG repeat ranged from 5 to 55 in normal FMR1 alleles, with the most prevalent alleles being 29 repeats (19.6%), followed by 30 repeats (13.04%) and 31 repeats (13.04%). Four of the 19 males (21.1%) presented with a full mutation (CGG repeats > 200) and were all classified as having a severe ID. Among the female participants 10/27 and 4/27 females had a premutation and a full mutation respectively, giving a carrier frequency for FXS of 51.8% among females. Nine of the 14 females who either had a premutation or a full mutation were normal (64.3%), while the rest (n = 5/14) had a mild ID. Of the 5 females with mild ID, 3 had a full mutation for FXS (> 200 CGG repeat), and the other 2 had a premutation (91, 101 CGG repeats) and presented with premature menopause.
Kharrat <i>et al.</i>	2020	Non-classical human leukocyte antigen class I in Tunisian children with autism.	15 families with one child having a diagnosis of ASD, for a total of 45 individuals and 15 ASD cases (4.5 ± 2 yrs; 13M, 2F).	ICD-10 and CARS.	DNA typing of HLA class I genes was performed using PCR-SSP and PCR-RFLP methods; serum levels of HLA-G (1 and 5) measured by a validated ELISA technique.	No association was found between any polymorphism and autism in the study subjects but parents carrying [GG] genotype presented a higher sHLA-G levels than those carrying ([CC]+[GC]) genotypes. Therefore, the investigated polymorphisms of HLA-G, -E, and -F genes did not lead to autism susceptibility in Tunisian children. However, the CGTIGA haplotype was found to be associated with the disease.
Meguid <i>et al.</i>	2020	Copy number variations of SHANK3 and related sensory profiles in Egyptian children with autism spectrum disorder.	40 ASD (3-5 yrs).	DSM-V, ADI-R, CARS and SSP.	SHANK3 CNVs were assessed using Multiplex Ligation-dependent Probe Amplification.	77.5 % of cases showed sensory reactivity symptoms. The greatest difference from normality was observed in the under-responsive/seeks sensation domain, followed by the tactile sensitivity domain, whereas hypo-activity (low-energy/weak domain) was closest to normal. The sensory reactivity symptoms were significantly correlated with the severity of ASD. However, only three of the 40 cases had de novo duplications at 22q13.33. The duplications included SHANK3 in two

						of the cases and only the distal flanking region of SHANK3 in the third case. All three duplication cases also showed symptoms associated with the low-energy/weak domain.
Saad <i>et al.</i>	2020	Polymorphism of interleukin-1 β and interleukin-1 receptor antagonist genes in children with autism spectrum disorders.	80 ASD (3.5–10 yrs; 65M, 15F) and 60 controls (3–9.5 yrs; 50M, 10F).	DSM-V, ADI-R and CARS.	Serum IL-1 β was assayed using a solid-phase Enzyme Amplified Sensitivity Immunoassay while IL-1RA was measured using a Human IL-1 RII Quantikine ELISA kit. Performed genotyping of the transcriptional start site of the IL-1 β genes.	Children with ASD had significantly higher levels of IL-1 β and IL-1RA and significantly higher frequencies of homozygous (CC) and heterozygous (TC) genotype variants of IL-1 β -511 and IL-1RA. The frequency of the IL-1 β -511 allele (C) was higher in the ASD group, the homozygous and heterozygous variants of IL-1RA allele II were also significantly higher in ASD. There was no significant association between the IL-1 β -31 genotype and autism classes. However, there were significant differences in the distribution of the IL-1RA heterogeneous genotype and allele II among children with severe autism. Polymorphisms in the IL-1 β -511 and IL-1RA genotype variants correlated positively with autism severity and behavioral abnormalities.
Stathopoulou <i>et al.</i>	2020	DNA methylation associated with mitochondrial dysfunction in a South African Autism Spectrum Disorder cohort.	93 ASD and 52 controls (6–12 yrs; 145M, 0F).	ADOS-2.	Measured DNA methylation with the Illumina 450 K MethylationArray, targeted next generation bisulfite sequencing and pyrosequencing. Urinary organic acid analysis was performed using gas chromatography–mass spectrometry.	898 genes were significantly DM between ASD cases and controls. These genes converged on 9 mitochondrial canonical pathways, and DM was validated for 52 CpG sites across 14 genes involved in mitochondrial function. Three metabolites were markedly elevated in ASD and these indicated evidence of oxidative stress.
Bam <i>et al.</i>	2021	DNA Methylation of PGC-1 α Is Associated With Elevated mtDNA Copy Number and Altered Urinary Metabolites in Autism Spectrum Disorder.	93 ASD and 52 controls (6–12 yrs; 145M, 0F).	ADOS-2.	DNA methylation was measured using targeted next generation bisulfite sequencing.	Significant DM was observed in six key genes converging on mitochondrial biogenesis, fission and fusion in ASD, namely PGC-1 α , STOML2, MFN2, FIS1, OPA1, and GABPA. Mitochondrial DNA (mtDNA) copy number, a marker of mitochondrial function, was elevated in ASD and correlated significantly with DNA methylation at the PGC1 α promoter. DNA methylation at PGC-1 α CpG#1 and mtDNA copy number correlated significantly with levels of urinary organic acids associated with mitochondrial dysfunction.
El-Ansary <i>et al.</i>	2021	GABA synaptopathy promotes the elevation of caspases 3 and 9 as pro-apoptotic markers in Egyptian patients with autism spectrum disorder.	20 ASD (3-4 yrs; 12M, 8F) and 20 age-matched controls (11M, 9F).	DSM-IV-TR, ADI-R, ADOS and Developmental, Dimensional, and Diagnostic Interview.	Measured plasma GABA, caspase 3 and 9 using a kit-based ELISA.	GABA level was reduced in ASD while levels of caspases 3 and 9 were significantly higher. ROC and predictiveness curves showed that caspases 3, caspases 9, and GABA might be utilized as predictive markers in autism diagnosis.
Higazi <i>et al.</i>	2021	Expression analysis of selected genes involved in tryptophan metabolic pathways in	45 ASD (4-10 yrs; 32M, 13F), 44 children with learning disabilities	The diagnosis of learning disabilities was performed through intelligence tests (IQ	Measured expression levels of the MAOA, HAAO and AADAT genes using real-time RT-qPCR.	Children with LDs and ASD had significantly lower haemoglobin, iron and vitamin D3 while ASD was associated with decreased zinc/copper ratios. There was a significant decrease in the expression levels of MAOA, HAAO and AADAT in ASD but not LDs.

		Egyptian children with Autism Spectrum Disorder and learning disabilities.	(6-13 yrs; 32M, 12F) and 40 controls (4-13 yrs; 22M, 18F).	tests), achievement tests, visual-motor integration tests and language tests. ASD children were diagnosed by DSM-5 criteria and CARS.	serum levels of iron, zinc and copper were assessed by colorimetric kits.	
Mostafa <i>et al.</i>	2021	Plasma levels of nerve growth factor in Egyptian autistic children: Relation to hyperserotonemia and autoimmunity.	22 ASD (4-12 yrs; 16M, 6F) and 22 controls (4-11 yrs; 17Ms, 5F).	DSM-V and CARS.	Serum serotonin levels were assayed by using the available serotonin EIA kit, serum anti-myelin basic protein antibodies were measured using an ELISA kit, F was measured using electro-chemiluminiscence.	Levels of NGF, serotonin and anti-MBP were significantly higher in autistic children than healthy control children. There was a significant positive correlation between NGF and serotonin levels in autistic patients. There was a non-significant correlation between serum levels of the studied laboratory parameters and both age of patients and results of CARS.
Omotosho <i>et al.</i>	2021	Oxidative stress indices in ASD children in Sub-Sahara Africa.	25 ASD (5.96 ± 1.40 years) and 25 controls (6.18 ± 2.59 years).	DSM-V.	Essential and toxic metals were analyzed using induction-coupled plasma-mass spectrometry (ICP-MS); oxidative stress markers [malondialdehyde (MDA), total plasma peroxidase (TPP), and total antioxidant capacity (TAC)] were determined using appropriate biochemical methods.	TPP and TAC were significantly reduced while MDA was higher in ASD. While the oxidative stress index was higher in ASD, this was not significant. Pb was significantly increased while Mg, Zn, and Cu levels were reduced in ASD. A significant negative correlation between Mg and OSI was observed in the controls. Reduction in Zn and Mg levels with a concurrent increase in Pb in children with ASD in this study may be the basis of inadequate TAC manifesting as increased MDA and reduced TPP levels.
Said <i>et al.</i>	2021	Role of glutathione-S-transferase M1 (GSTM1) and T1 (GSTT1) genes on aluminum concentration and oxidative markers among autistic children.	76 ASD (2-8 yrs; 62M, 14F) and 30 controls (7.23 ± 0.858 yrs; 23M, 7F).	DSM-V, full medical history and clinical examination.	Levels of aluminum in hair was determined using Inductively Coupled Optical Emission Spectrometer. PCR was used to screen for GST gene polymorphisms. Glutathione -S- transferase enzyme activity and levels of serum malondialdehyde (MDA) and nitric oxide were measured using colourimetric assays.	The null GSTM1 and GSTT1 genotype was the most common type in ASD. There is marked increase in aluminum concentrations in hair of ASD children and oxidative markers (increase in MDA and NO) leading to oxidative damage.
Abdel <i>et al.</i>	2022	Study of serum neopterin in children with attention deficit hyperactivity disorder	25 ASD (13M, 12F) and 25 ADHD (19M, 6F) (3-15 yrs) and 25 age-	Conner's Parent Rating Scale- Revised- Long version, CARS.	Serum neopterin levels were measured by using commercially enzyme	NS difference in mean neopterin serum level between cases and controls or within ADHD subgroups, and neopterin did not correlate with ASD severity. In ASD, but not controls or ADHD, there was a moderate significant negative correlation between neopterin and age.

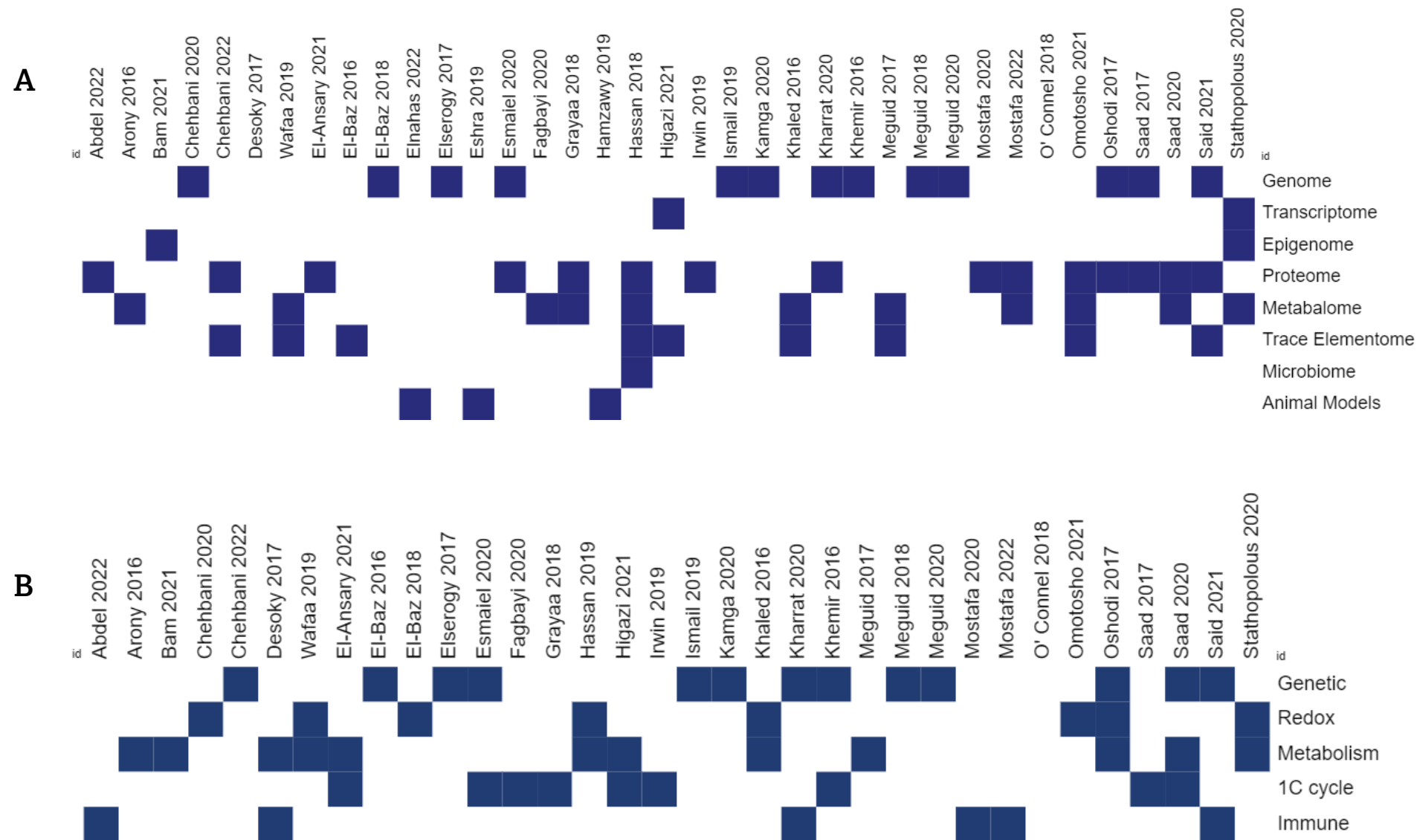
		and autistic spectrum disorder: Fayoum Governorate, Egypt.	and gender-matched controls.		linked immunoassay (ELISA) kit.	
Chehbani <i>et al.</i>	2022	Yield of array-CGH analysis in Tunisian children with autism spectrum disorder.	98 ASD, (3-18yrs; 83M, 15F) belonging to 91 simplex and four multiplex families.	DSM-IV, ADI-R, ADOS-2, CARS.	Microarray-based comparative genomic hybridization (aCGH) technology (using the Human Genome CGH SurePrint G3 Microarray 4 × 180 K Kit).	11 (11.2%) patients, including three females and eight males, carry a total of 14 “pathogenic” or “likely pathogenic” CNVs, encompassing 10 duplications and four deletions. Rare CNVs of “uncertain clinical significance” were detected in 26 (26.5%) patients; “Likely benign” and “benign” CNVs were detected in 37 (37.8%) patients and 24 (24.5%) patients, respectively. 5 individuals carry rare “pathogenic” or “likely pathogenic” dup/dels. GSEA of CNVs showed enrichment for Synapse, Neuron Differentiation, Synaptic Signaling, Neurogenesis, Regulation of Trans-synaptic Signaling, Synaptic Growth at Neuromuscular Junction, Neuron Projection, and Signaling Adaptor Activity.
Elnahas <i>et al.</i>	2022	Novel role of peroxisome proliferator activated receptor- α in valproic acid rat model of autism: Mechanistic study of risperidone and metformin monotherapy versus combination.	VPA rat model for ASD; with metformin or risperidone treatment.	Three-chamber sociability test, Marble burying test, Tail-immersion nociceptive test, Open field test, Morris water maze test.	NF- κ B, TNF- α and IL-1 β were measured by ELISA. Reduced glutathione (GSH) levels, Catalase (CAT) activity, lipid peroxidation “Malondialdehyde” (MDA) and nitric oxide (NO), as NO metabolites ‘NOx’ (nitrite levels) were measured using commercially available colorimetric assay kits. PPAR- α expression was measured using RT-QPCR. Caspase-3 and GFAP were measured using immunohistochemistry.	Prenatal VPA exposure increased ASD-like behaviors and decreased PPAR- α expression. VPA significantly induced neuroinflammation and redox imbalance manifested by altered inflammatory markers (TNF- α , IL-1 β and NF- κ B) and oxidative/nitrosative stress markers (reduced GSH and CAT activity with elevated MDA and NOx). Prenatal VPA induced apoptosis and reactive astrogliosis expressed by increased mean area % of caspase-3 and GFAP immune reaction respectively. Both MET and RIS either monotherapy or in combination were able to reverse these changes. The effect of MET was comparable to RIS. Moreover, MET was able to alleviate the RIS induced weight gain and improve cognitive functions highlighting its promising adjunctive role in alleviating ASD pathophysiology.
Mostafa <i>et al.</i>	2022	Up-regulated serum levels of TAM receptor tyrosine kinases in a group of Egyptian autistic children.	30 ASD (3.5 -11 years) and 30 age and sex-matched controls.	DSM-V, CARS.	Serum TAMRTKs were measured by using the commercially available Enzyme-linked immunosorbent Assay (ELISA) kits.	Serum levels of TAMRTKs were significantly higher in autistic children than healthy control children. Patients with severe autism had significantly higher serum levels of Tyro3, Axl and Mer than patients with mild to moderate autism and CARS scores correlated significantly with serum TARMTKs.

Table S2: First Author and Year of Publication for 85 ASD Studies across Eight Thematic Focus Areas Published from SA between 2016–2022

Family and Social	Clinical/ Phenotyping/ Behavioral
Meiring 2016	Hoogenhout 2016
Pottas 2016	Fourie 2017
Schlebusch 2016	Hoogenhout 2017
Cole 2017	Leclezio 2018
Schlebusch 2017	Naidoo 2018
Van Der Merwe 2017	Viviers 2020
Wetherston 2017	Adams 2021
Alhazmi 2018	Herdien 2021
Clasquin-Johnson 2018	Ringshaw 2021
Dawson-Squibb 2018	Adams 2022
Mthombeni 2018	Ringshaw 2022
Schlebusch 2018	Scholtz 2022
Makombe 2019	Shuffrey 2022
Ramseur 2019	Diagnosis
Reddy 2019	Chambers 2017
Viljoen 2019	Smith 2017
Adams 2020	Chambers 2018
Britz 2020	Franz 2018
Dawson-Squibb 2020	van Biljon 2019
Leigh 2020	Lupindo 2022
Mazibuko 2020	Vorster 2021
Simelane 2020	Vorster 2022
Soeker 2020	Zieff 2022
Adams 2021	Education
Mupaku 2021	Hutton 2016
Adams 2022	Mithimunye 2018
Carter 2022	Erasmus 2019
Erasmus 2022	de Jager 2020
Guler 2022	Murray 2020
Kehinde 2022	Numisi 2020
Mokoena 2022	Erasmus 2021
Okwara 2022	Sefotho 2021
Pillay 2022	Nthibeli 2022
Soeker 2022	Pillay 2022
Professional Knowledge	Pillay 2022
Krynauw 2018	Interventions/Treatment
Wium 2018	
Naidoo 2020	Wallace 2016
Lee Evetts 2021	Guler 2018
Araujo 2022	Hampton 2019
Moroe 2022	Franz 2022

Prevalence/Demographics	Karrim 2022
Erasmus 2019	Molecular
Rasdien 2019	O'Connell 2018
Pillay 2021	Stathopoulos 2020
Pillay 2021	Bam 2021

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Online Resource 2: Figure S1. A) Level of molecular regulation explored by all 37 molecular autism studies from Africa published between 2016 – 2022. B) African cohort studies published between 2016-2022 categorized according to mechanisms of interest.