

Biofluid	Country	Study population	Targeted/Untargeted sequencing technique	Statistics	Biomarker panel and Evaluation	Reference
Plasma	China	CNV (n = 67), PCV (n = 60) and control (n = 50)	Untargeted LC-MS/MS	Variance analysis and the chi-square test	17 differential metabolites.	14
Plasma	America	IAMD (n = 91), NVAMD (n = 100), and non-AMD controls (n = 195).	Untargeted LC-MS and LC-MS/MS	Kruskal–Wallis (KW)	158 metabolic features. The 10-fold cross-validation balanced accuracy rate using these discriminatory features was 77.8%.	6
RPE	America	cultured RPE from donor normal eyes (n = 3) and AMD RPE (n = 4)	Untargeted LC-MS	Student's t test	-	21
Plasma	America	NVAMD (n = 100) and control (n = 192)	Untargeted LC-MS and LC-MS/MS	Nested feature selection	159 identified metabolic features. The 159 features produced a 10-fold cross-validation balanced accuracy rate of 96.1% in the training set and a balanced accuracy rate of 75.6% along with an area under the curve (AUC) of 0.83 in the test set.	7
Plasma	America	Early AMD, intermediate AMD, late AMD (n = 89) and control (n = 30)	Targeted UPLC-MS	Logistic regression analysis	87 metabolites. ROC analysis (area under the ROC curve, 0.80; 95% confidence interval, 0.71–0.90).	8
Plasma	USA	Two cohort AMD (n = 391) and control (n = 100)	Untargeted UPLC-MS	Logistic regression models	69 metabolites. (Stage+2Eye model) (AUC = 0.815; 95% CI: 0.771–0.860) and the model comparing patients with AMD versus controls (AMD/	9

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Supplemental Table 2: Relevant Metabolomics Studies Included in Our Study.

AMD: age-related macular degeneration; PCV: polypoidal choroidal vasculopathy; NVAMD: neovascular age-related macular degeneration; IAMD: intermediate age-related macular degeneration; RPE: retinal pigment epithelial; LC-MS: liquid chromatography-mass spectrometry; UPLC: ultra-performance liquid chromatography; TOF: time of flight; Q-TOF, quadrupole-time of flight; FTMS: fouriertransform mass spectrometry; GC: gas chromatography; PLS-DA: partial least squares discriminant analysis; OPLS-DA; orthogonal partial least squares discriminant analysis; NMR: nuclear magnetic resonance; ANOVA; one-way analysis of variance.

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