Supplementary：

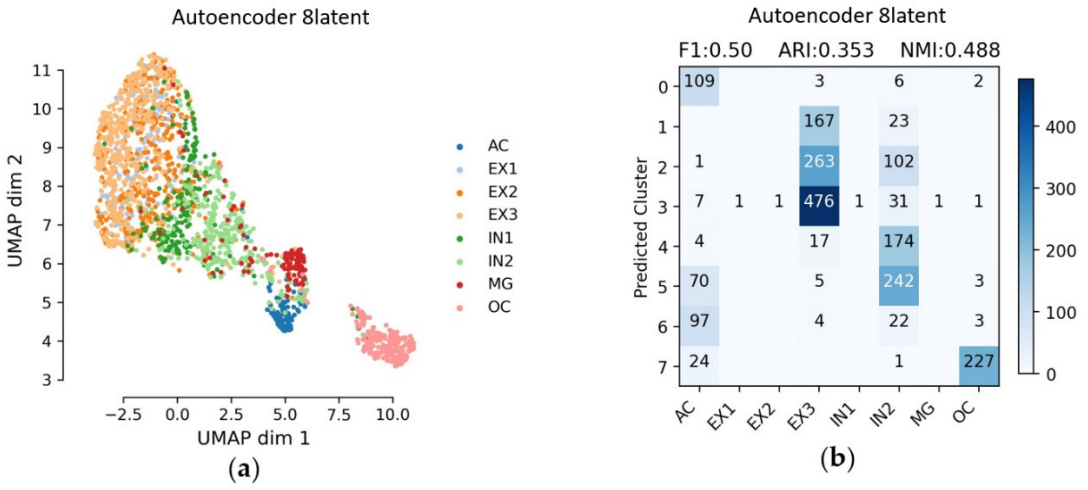

Figure S1. Feature embedding and clustering of General autoencoder under different 8 latent space. Clustering accuracy was shown in evaluation matrices between cluster assignments predicted by K-means and the reference cell types. The blue colorbar refers to the number of cells; (a) UMAP visualization of the extracted features from General autoencoder with 8 latent features; (b) Evaluation matrices with 8 latent features.

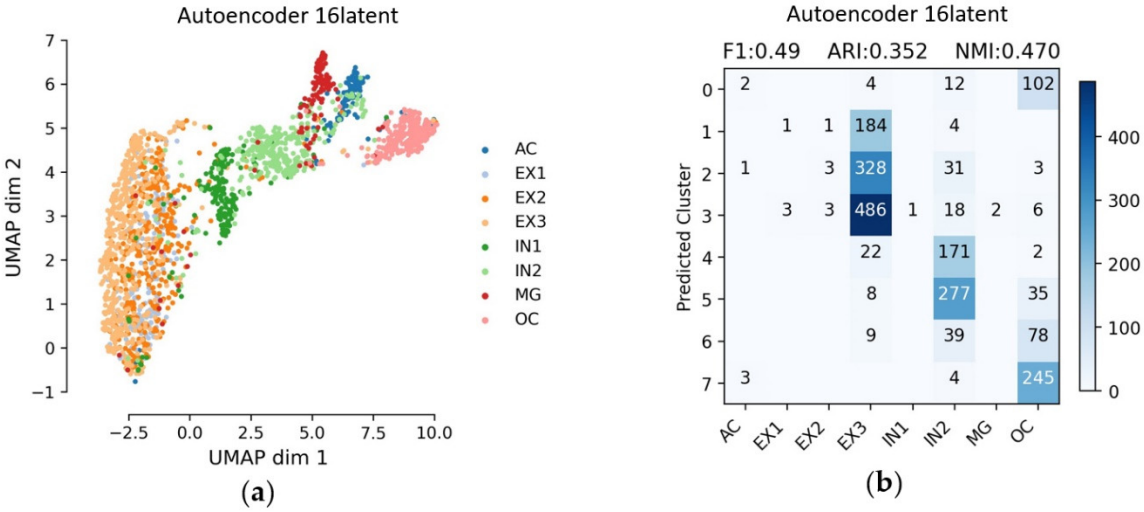

Figure S2. Feature embedding and clustering of General autoencoder under different 16 latent space. Clustering accuracy was shown in evaluation matrices between cluster assignments predicted by K-means and the reference cell types. The blue colorbar refers to the number of cells; (a) UMAP visualization of the extracted features from General autoencoder with 16 latent features; (b) Evaluation matrices with 16 latent features.

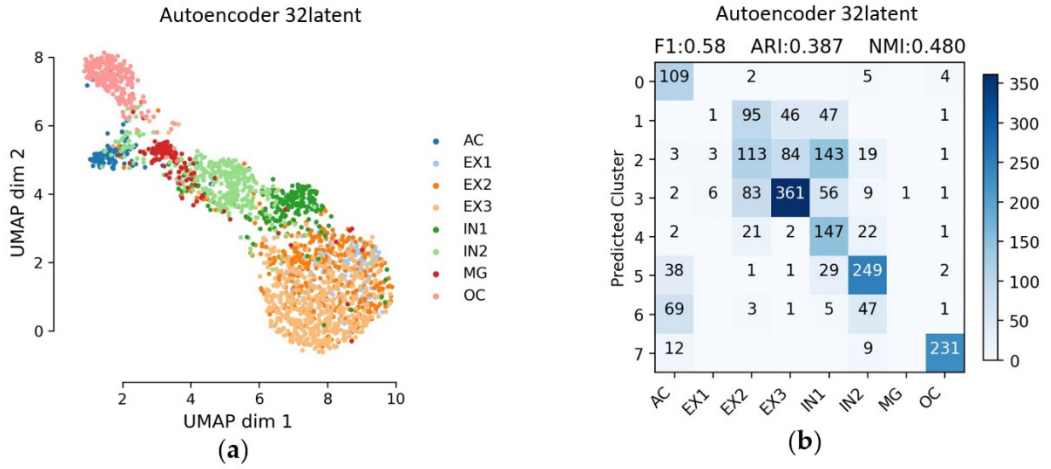

Figure S3. Feature embedding and clustering of General autoencoder under different 32 latent space. Clustering accuracy was shown in evaluation matrices between cluster assignments predicted by K-means and the reference cell types. The blue colorbar refers to the number of cells; (a) UMAP visualization of the extracted features from General autoencoder with 32 latent features; (b) Evaluation matrices with 32 latent features.

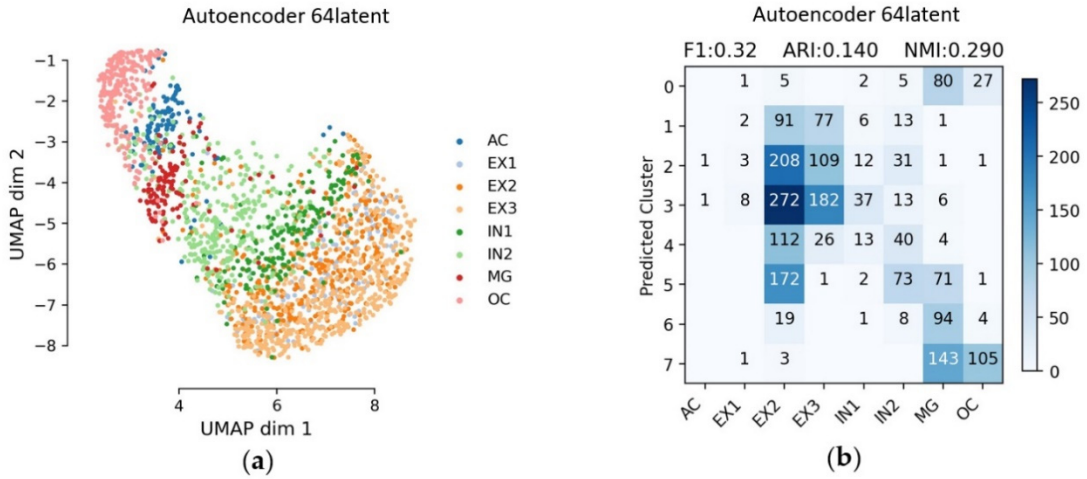

Figure S4. Feature embedding and clustering of General autoencoder under different 64 latent space. Clustering accuracy was shown in evaluation matrices between cluster assignments predicted by K-means and the reference cell types. The blue colorbar refers to the number of cells; (a) UMAP visualization of the extracted features from General autoencoder with 64 latent features; (b) Evaluation matrices with 64 latent features.

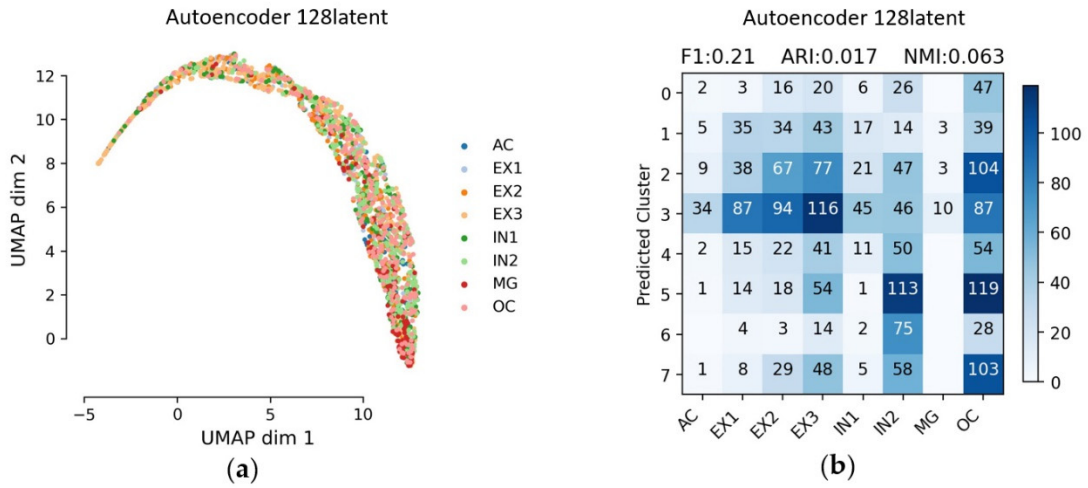

Figure S5. Feature embedding and clustering of General autoencoder under different 128 latent space. Clustering accuracy was shown in evaluation matrices between cluster assignments predicted by K-means and the reference cell types. The blue colorbar refers to the number of cells; (a) UMAP visualization of the extracted features from General autoencoder with 128 latent features; (b) Evaluation matrices with 128 latent features.

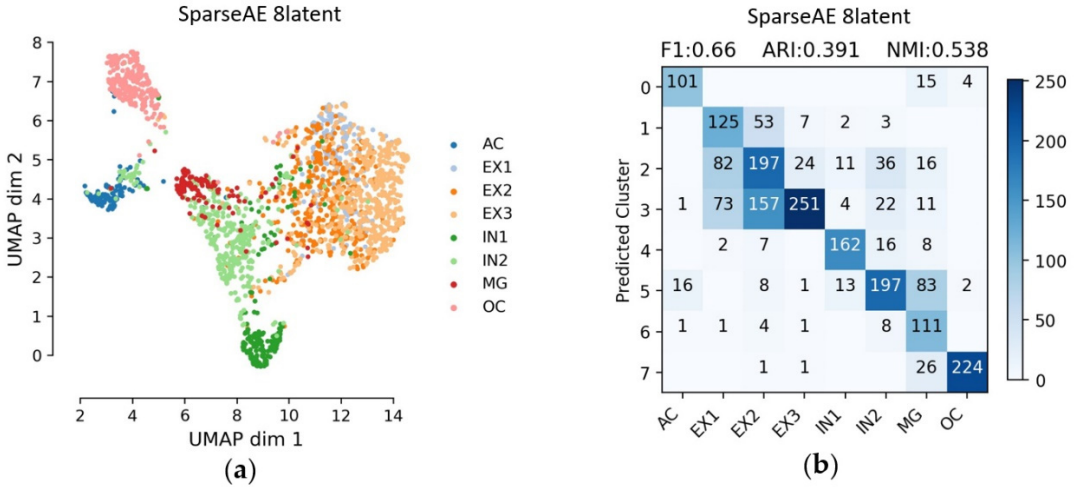

Figure S6. Feature embedding and clustering of SparseAE under different 8 latent space. Clustering accuracy was shown in evaluation matrices between cluster assignments predicted by K-means and the reference cell types. The blue colorbar refers to the number of cells; (a) UMAP visualization of the extracted features from SparseAE with 8 latent features; (b) Evaluation matrices with 8 latent features.

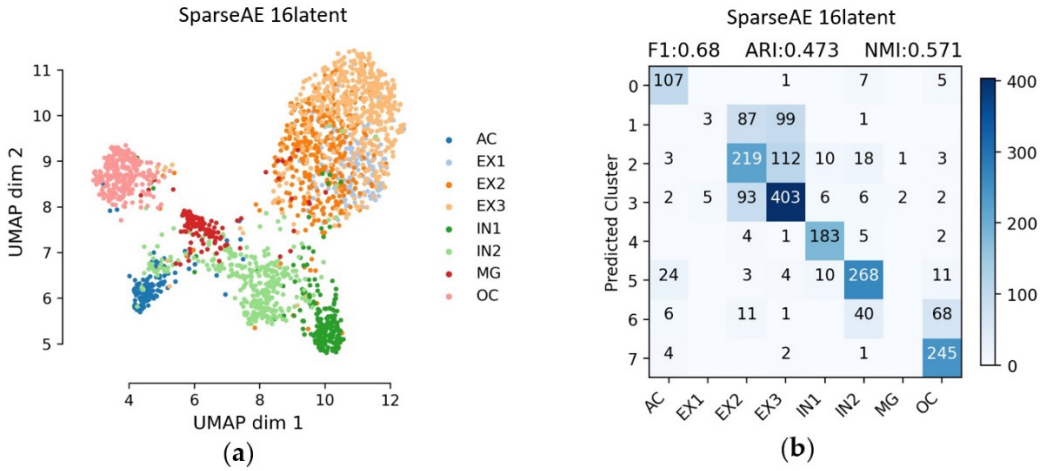

Figure S7. Feature embedding and clustering of SparseAE under different 16 latent space. Clustering accuracy was shown in evaluation matrices between cluster assignments predicted by K-means and the reference cell types. The blue colorbar refers to the number of cells; (a) UMAP visualization of the extracted features from SparseAE with 16 latent features; (b) Evaluation matrices with 16 latent features.

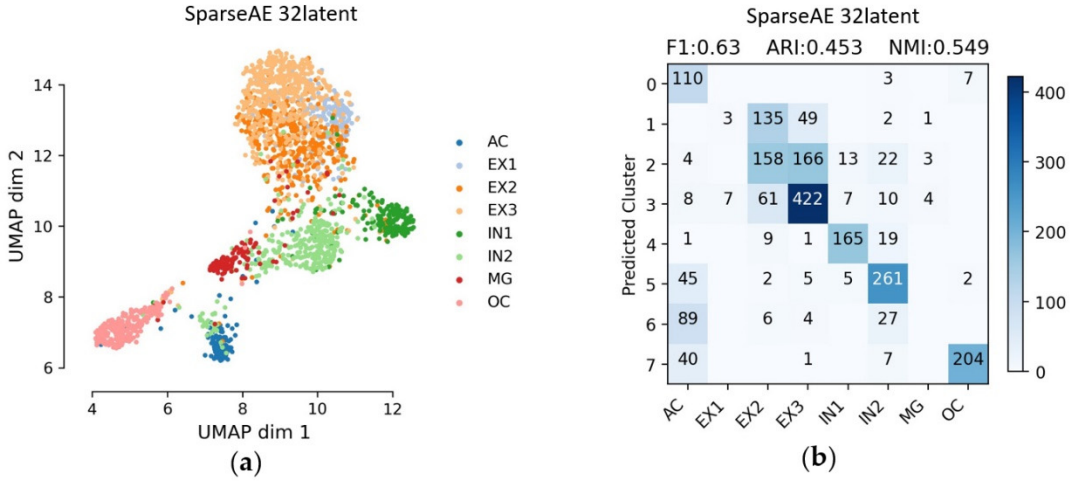

Figure S8. Feature embedding and clustering of SparseAE under different 32 latent space. Clustering accuracy was shown in evaluation matrices between cluster assignments predicted by K-means and the reference cell types. The blue colorbar refers to the number of cells; (a) UMAP visualization of the extracted features from SparseAE with 32 latent features; (b) Evaluation matrices with 32 latent features.

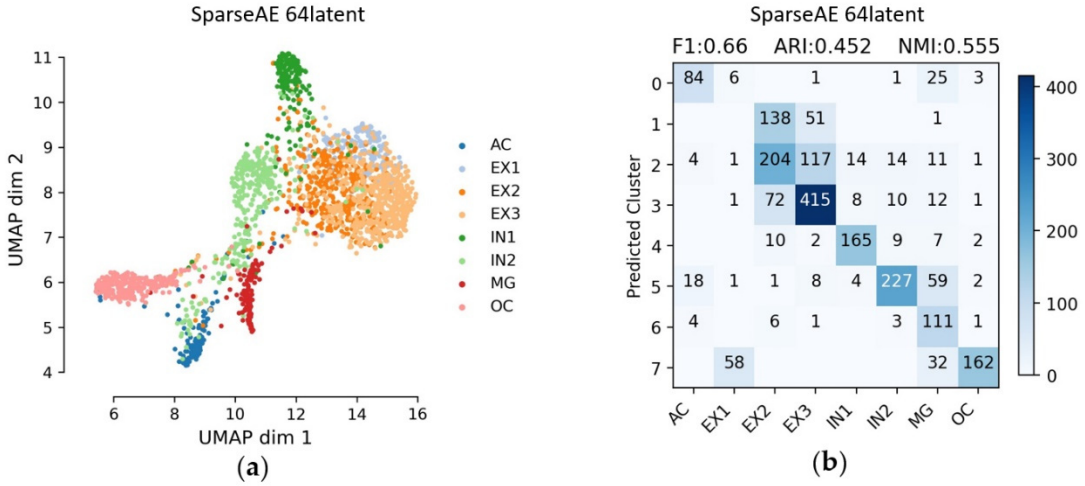

Figure S9. Feature embedding and clustering of SparseAE under different 64 latent space. Clustering accuracy was shown in evaluation matrices between cluster assignments predicted by K-means and the reference cell types. The blue colorbar refers to the number of cells; (a) UMAP visualization of the extracted features from SparseAE with 64 latent features; (b) Evaluation matrices with 64 latent features.

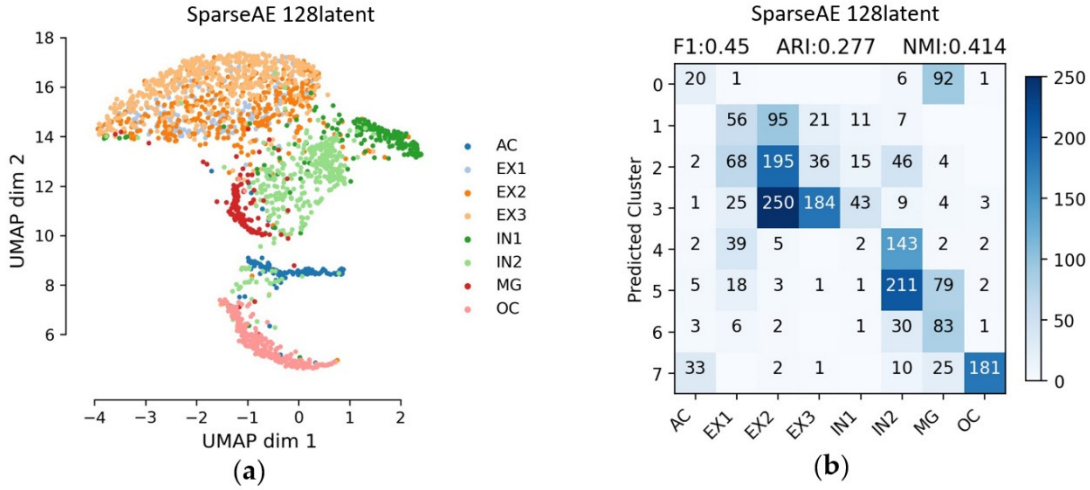

Figure S10. Feature embedding and clustering of SparseAE under different 128 latent space. Clustering accuracy was shown in evaluation matrices between cluster assignments predicted by K-means and the reference cell types. The blue colorbar refers to the number of cells; (a) UMAP visualization of the extracted features from SparseAE with 128 latent features; (b) Evaluation matrices with 128 latent features.

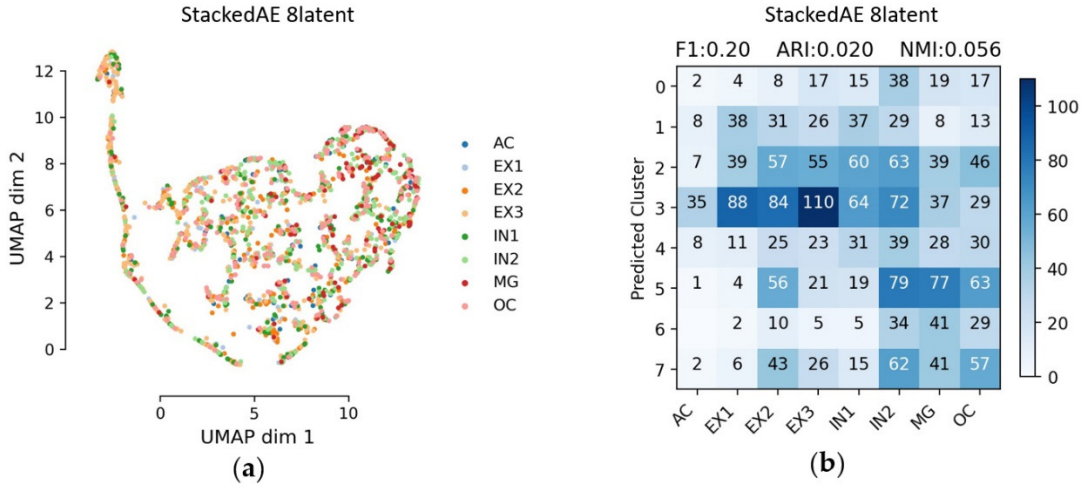

Figure S11. Feature embedding and clustering of StackedAE under different 8 latent space. Clustering accuracy was shown in evaluation matrices between cluster assignments predicted by K-means and the reference cell types. The blue colorbar refers to the number of cells; (a) UMAP visualization of the extracted features from StackedAE with 8 latent features; (b) Evaluation matrices with 8 latent features.

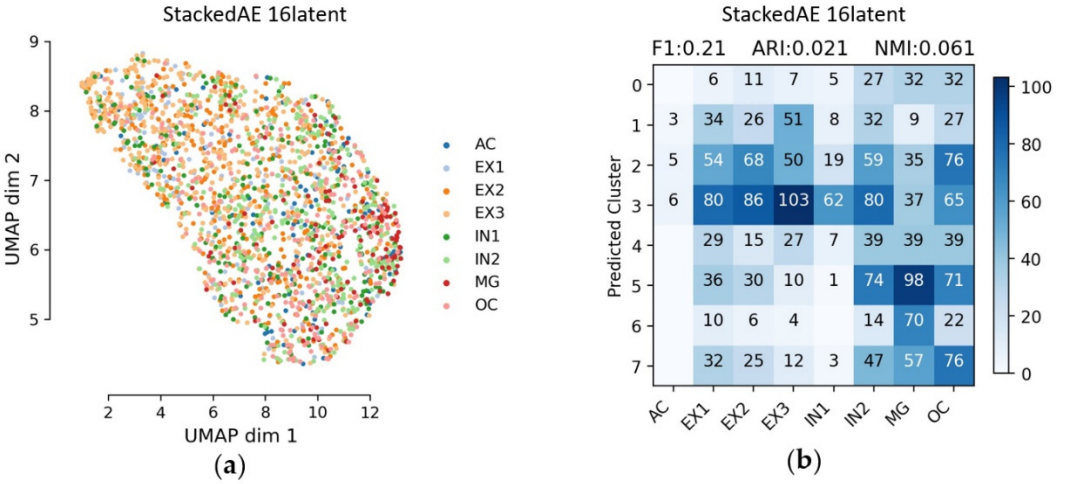

Figure S12. Feature embedding and clustering of StackedAE under different 16 latent space. Clustering accuracy was shown in evaluation matrices between cluster assignments predicted by K-means and the reference cell types. The blue colorbar refers to the number of cells; (a) UMAP visualization of the extracted features from StackedAE with 16 latent features; (b) Evaluation matrices with 16 latent features.

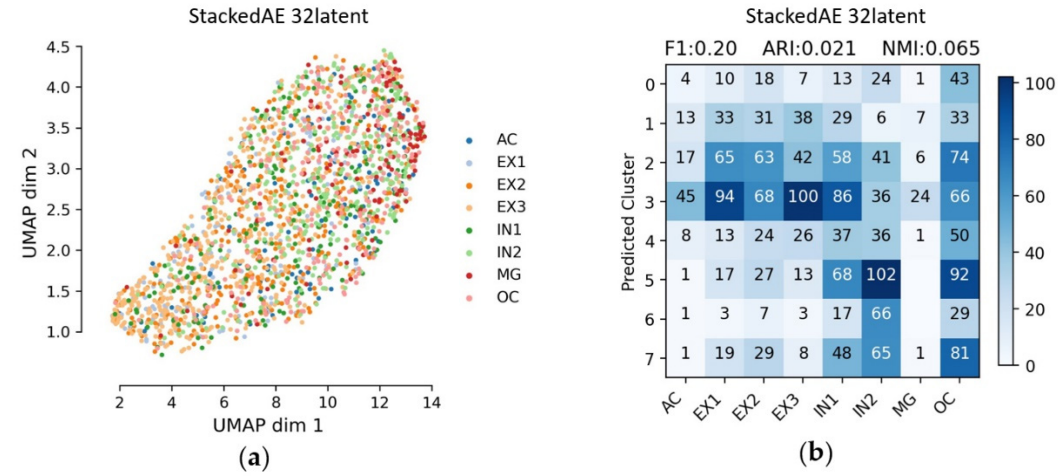

Figure S13. Feature embedding and clustering of StackedAE under different 32 latent space. Clustering accuracy was shown in evaluation matrices between cluster assignments predicted by K-means and the reference cell types. The blue colorbar refers to the number of cells; (a) UMAP visualization of the extracted features from StackedAE with 32 latent features; (b) Evaluation matrices with 32 latent features.

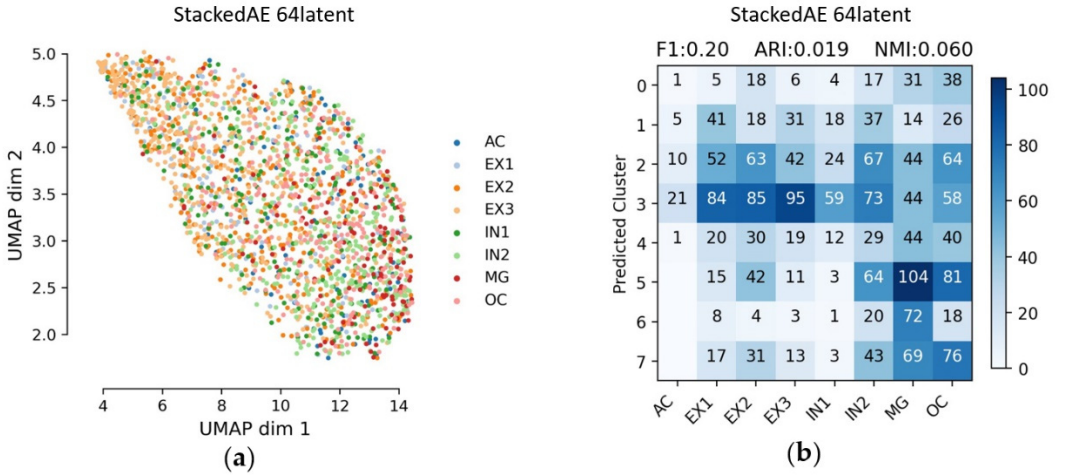

Figure S14. Feature embedding and clustering of StackedAE under different 64 latent space. Clustering accuracy was shown in evaluation matrices between cluster assignments predicted by K-means and the reference cell types. The blue colorbar refers to the number of cells; (a) UMAP visualization of the extracted features from StackedAE with 64 latent features; (b) Evaluation matrices with 64 latent features.

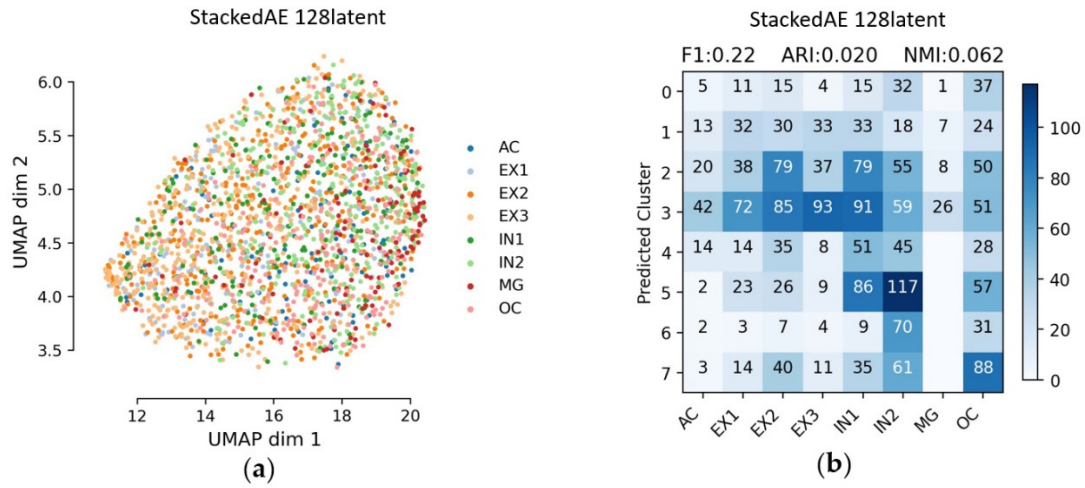

Figure S15. Feature embedding and clustering of StackedAE under different 128 latent space. Clustering accuracy was shown in evaluation matrices between cluster assignments predicted by K-means and the reference cell types. The blue colorbar refers to the number of cells; (a) UMAP visualization of the extracted features from StackedAE with 128 latent features; (b) Evaluation matrices with 128 latent features.

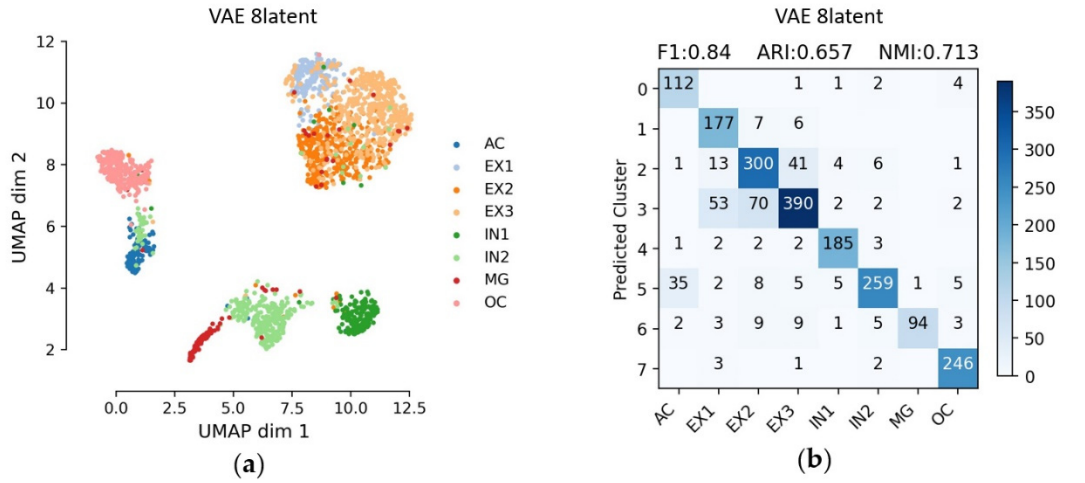

Figure S16. Feature embedding and clustering of VAE under different 8 latent space. Clustering accuracy was shown in evaluation matrices between cluster assignments predicted by K-means and the reference cell types. The blue colorbar refers to the number of cells; (a) UMAP visualization of the extracted features from VAE with 8 latent features; (b) Evaluation matrices with 8 latent features.

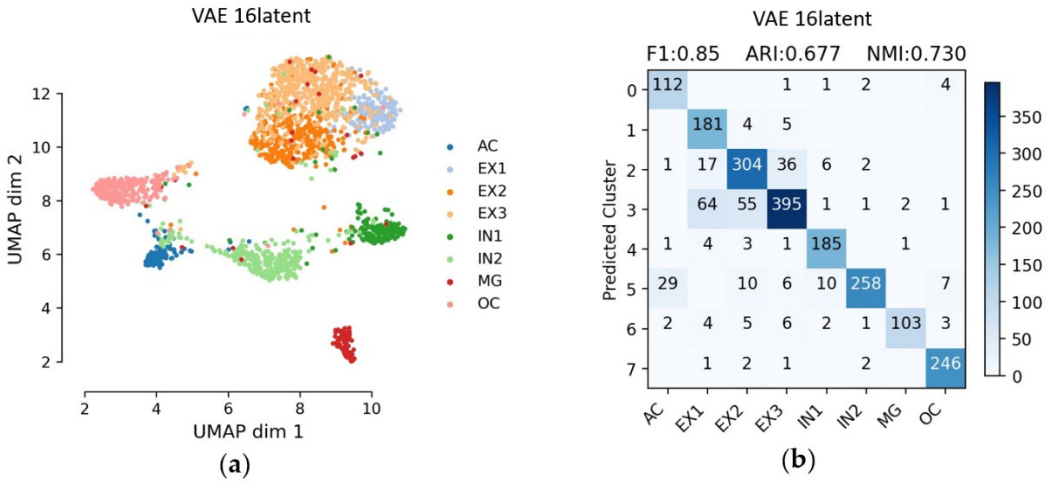

Figure S17. Feature embedding and clustering of VAE under different 16 latent space. Clustering accuracy was shown in evaluation matrices between cluster assignments predicted by K-means and the reference cell types. The blue colorbar refers to the number of cells; (a) UMAP visualization of the extracted features from VAE with 16 latent features; (b) Evaluation matrices with 16 latent features.

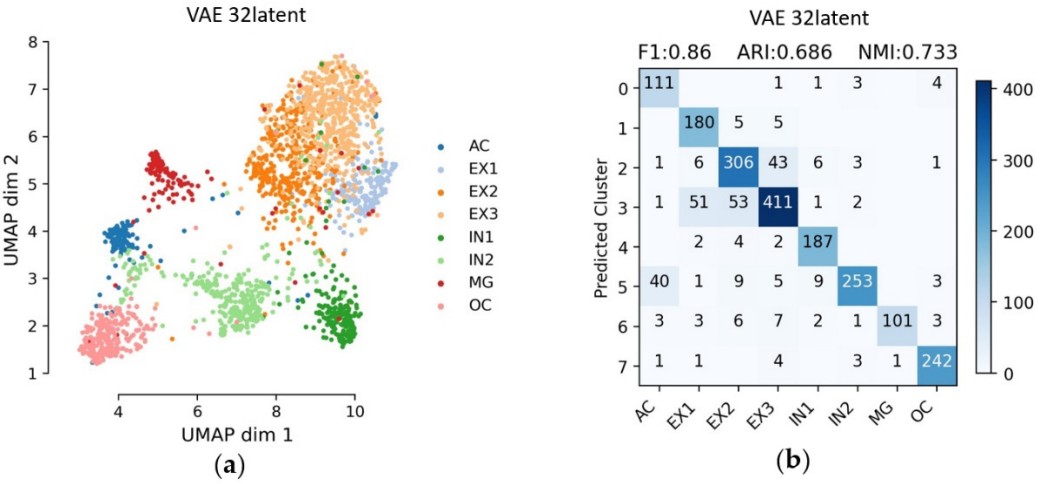

Figure S18. Feature embedding and clustering of VAE under different 32 latent space. Clustering accuracy was shown in evaluation matrices between cluster assignments predicted by K-means and the reference cell types. The blue colorbar refers to the number of cells; (a) UMAP visualization of the extracted features from VAE with 32 latent features; (b) Evaluation matrices with 32 latent features.

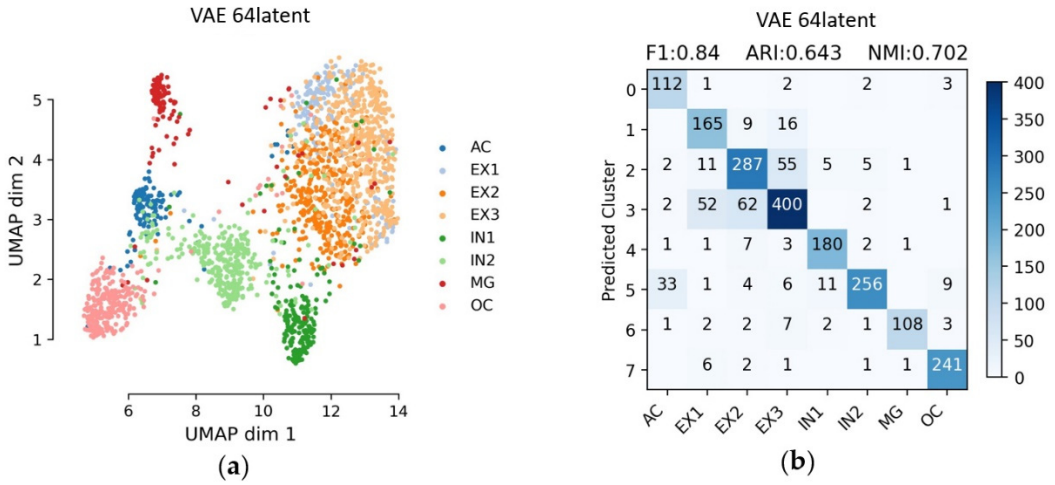

Figure S19. Feature embedding and clustering of VAE under different 64 latent space. Clustering accuracy was shown in evaluation matrices between cluster assignments predicted by K-means and the reference cell types. The blue colorbar refers to the number of cells; (a) UMAP visualization of the extracted features from VAE with 64 latent features; (b) Evaluation matrices with 64 latent features.

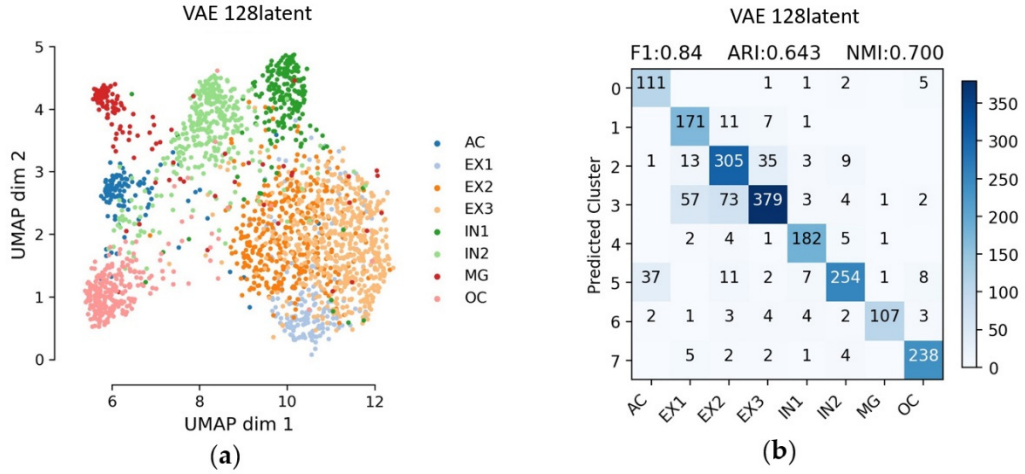

Figure S20. Feature embedding and clustering of VAE under different 128 latent space. Clustering accuracy was shown in evaluation matrices between cluster assignments predicted by K-means and the reference cell types. The blue colorbar refers to the number of cells; (a) UMAP visualization of the extracted features from VAE with 128 latent features; (b) Evaluation matrices with 128 latent features.

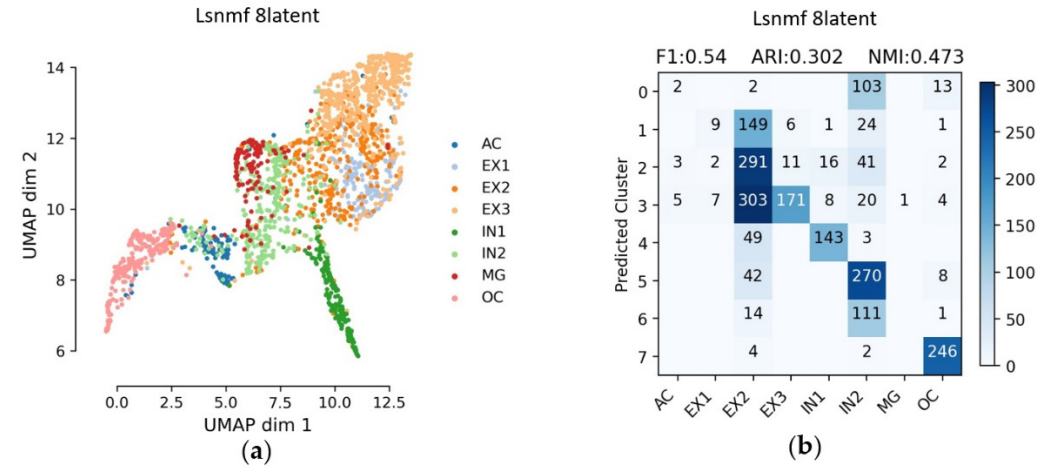

Figure S21. Feature embedding and clustering of Lsnmf under different 8 latent space. Clustering accuracy was shown in evaluation matrices between cluster assignments predicted by K-means and the reference cell types. The blue colorbar refers to the number of cells; (a) UMAP visualization of the extracted features from Lsnmf with 8 latent features; (b) Evaluation matrices with 8 latent features.

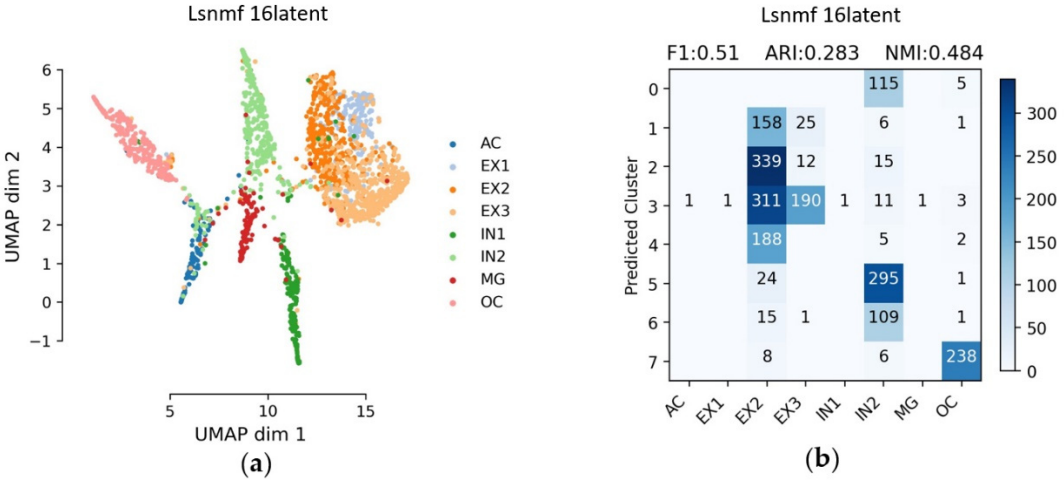

Figure S22. Feature embedding and clustering of Lsnmf under different 16 latent space. Clustering accuracy was shown in evaluation matrices between cluster assignments predicted by K-means and the reference cell types. The blue colorbar refers to the number of cells; (a) UMAP visualization of the extracted features from Lsnmf with 16 latent features; (b) Evaluation matrices with 16 latent features.

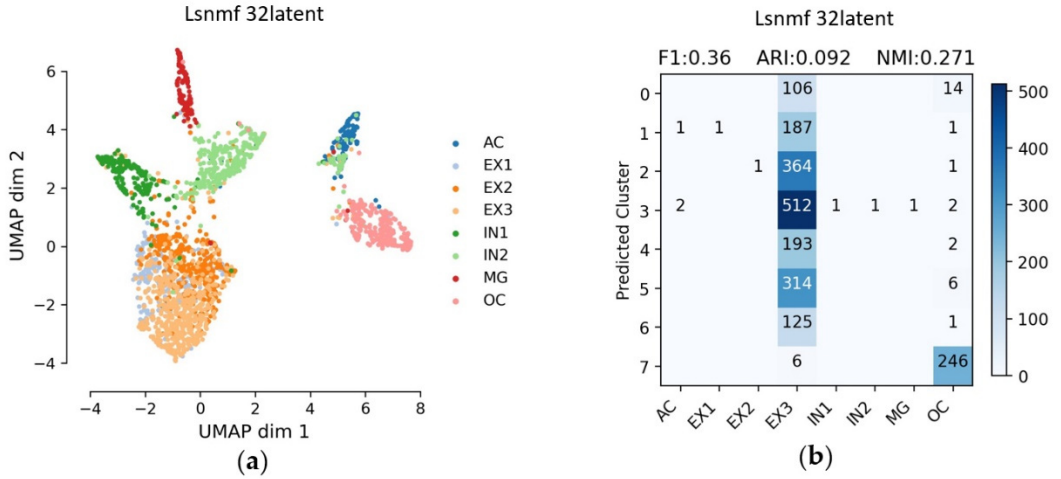

Figure S23. Feature embedding and clustering of Lsnmf under different 32 latent space. Clustering accuracy was shown in evaluation matrices between cluster assignments predicted by K-means and the reference cell types. The blue colorbar refers to the number of cells; (a) UMAP visualization of the extracted features from Lsnmf with 32 latent features; (b) Evaluation matrices with 32 latent features.

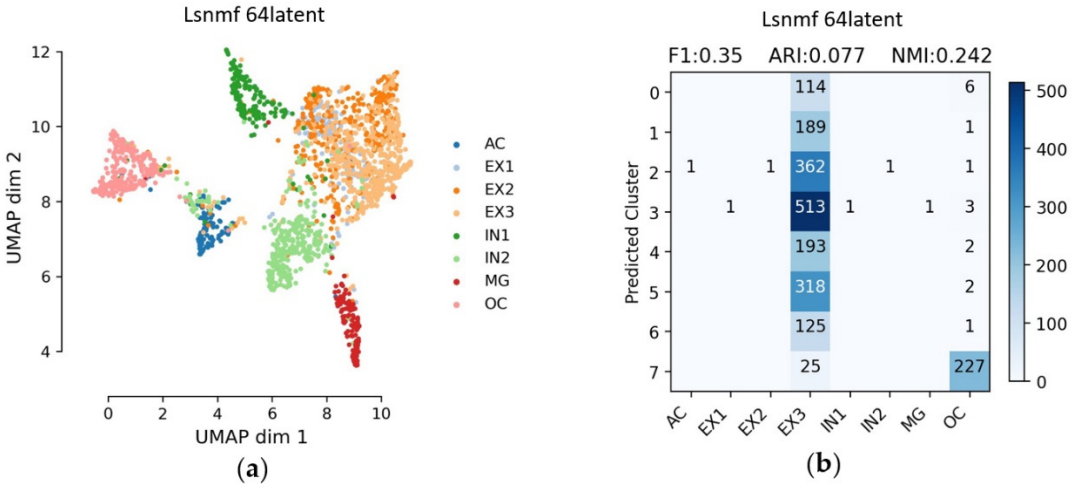

Figure S24. Feature embedding and clustering of Lsnmf under different 64 latent space. Clustering accuracy was shown in evaluation matrices between cluster assignments predicted by K-means and the reference cell types. The blue colorbar refers to the number of cells; (a) UMAP visualization of the extracted features from Lsnmf with 64 latent features; (b) Evaluation matrices with 64 latent features.

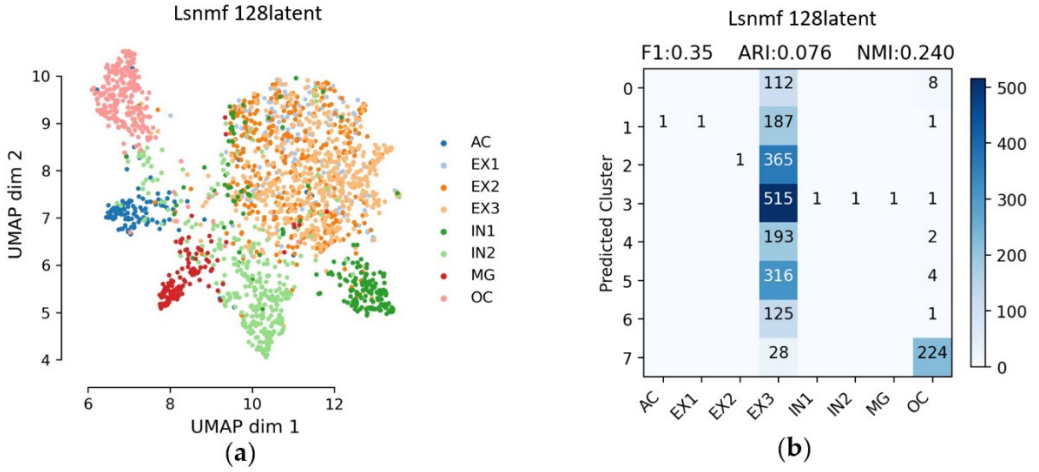

Figure S25. Feature embedding and clustering of Lsnmf under different 128 latent space. Clustering accuracy was shown in evaluation matrices between cluster assignments predicted by K-means and the reference cell types. The blue colorbar refers to the number of cells; (a) UMAP visualization of the extracted features from Lsnmf with 128 latent features; (b) Evaluation matrices with 128 latent features.

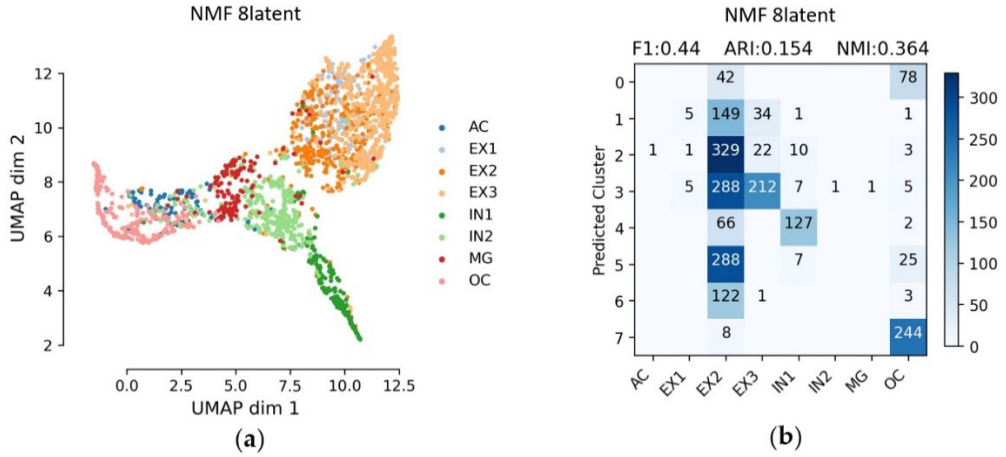

Figure S26. Feature embedding and clustering of NMF under different 8 latent space. Clustering accuracy was shown in evaluation matrices between cluster assignments predicted by K-means and the reference cell types. The blue colorbar refers to the number of cells; (a) UMAP visualization of the extracted features from NMF with 8 latent features; (b) Evaluation matrices with 8 latent features.

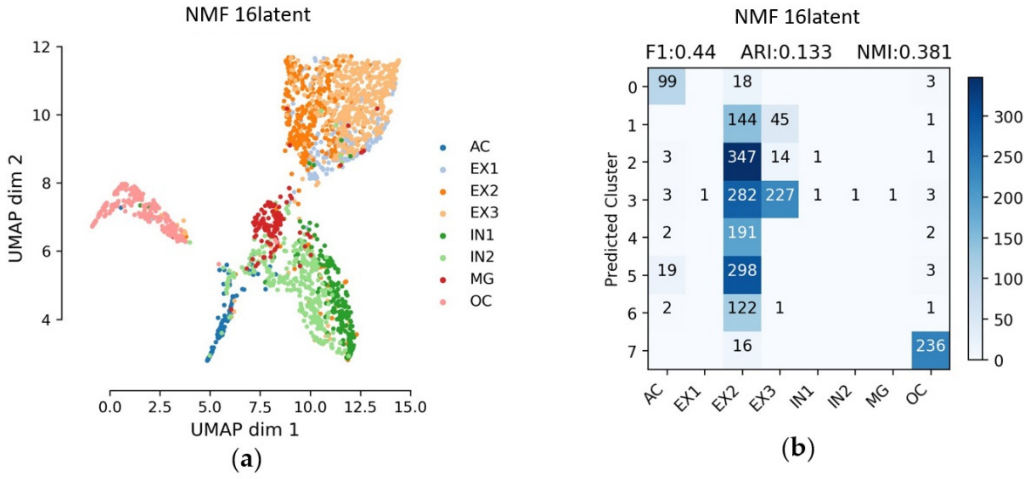

Figure S27. Feature embedding and clustering of NMF under different 16 latent space. Clustering accuracy was shown in evaluation matrices between cluster assignments predicted by K-means and the reference cell types. The blue colorbar refers to the number of cells; (a) UMAP visualization of the extracted features from NMF with 16 latent features; (b) Evaluation matrices with 16 latent features.

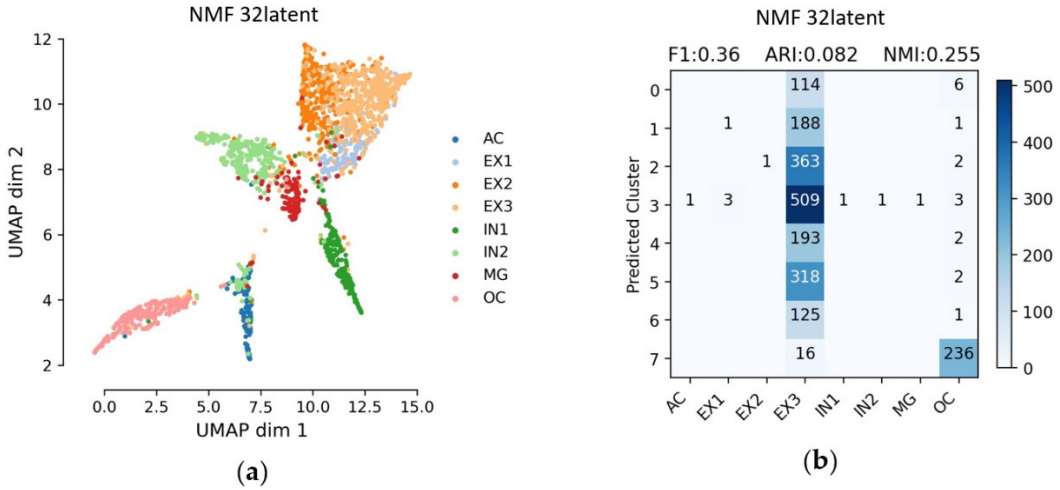

Figure S28. Feature embedding and clustering of NMF under different 32 latent space. Clustering accuracy was shown in evaluation matrices between cluster assignments predicted by K-means and the reference cell types. The blue colorbar refers to the number of cells; (a) UMAP visualization of the extracted features from NMF with 32 latent features; (b) Evaluation matrices with 32 latent features.

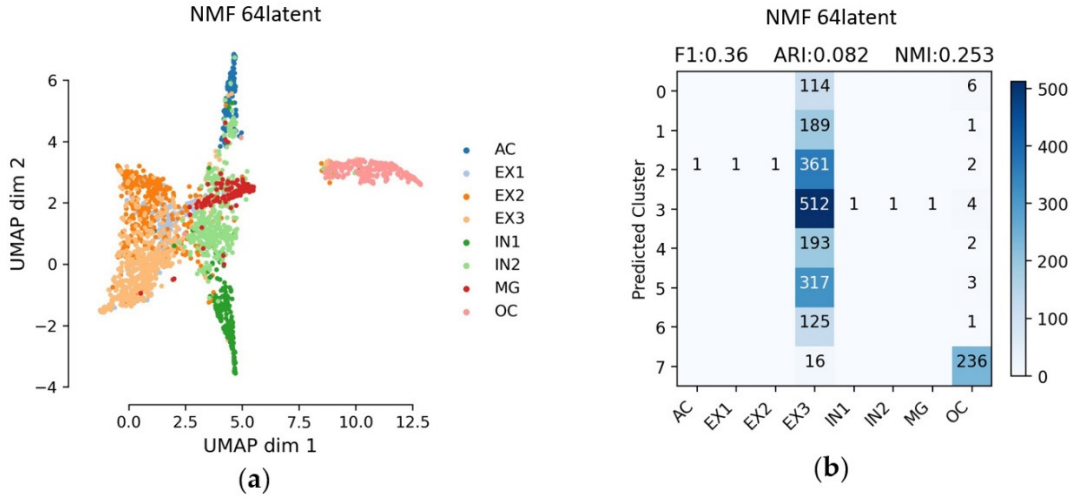

Figure S29. Feature embedding and clustering of NMF under different 64 latent space. Clustering accuracy was shown in evaluation matrices between cluster assignments predicted by K-means and the reference cell types. The blue colorbar refers to the number of cells; (a) UMAP visualization of the extracted features from NMF with 64 latent features; (b) Evaluation matrices with 64 latent features.

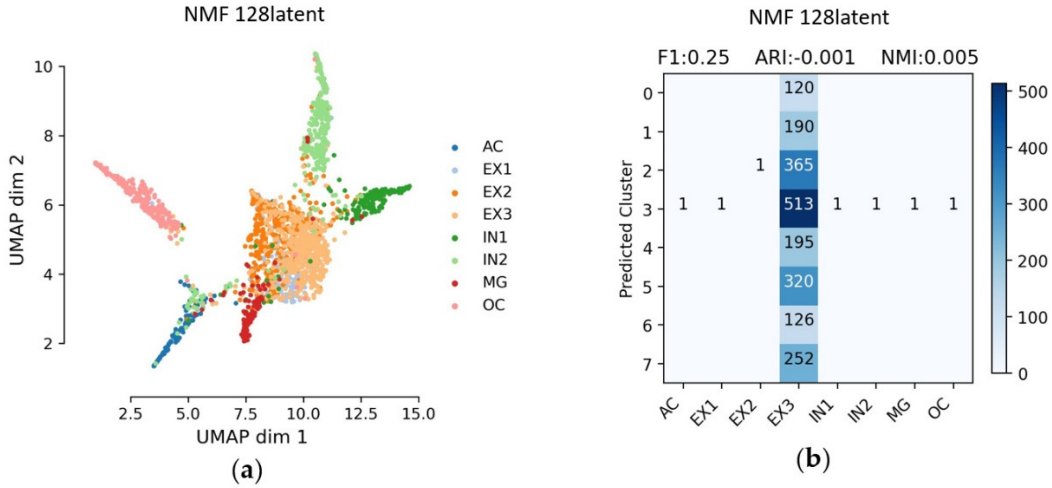

Figure S30. Feature embedding and clustering of NMF under different 128 latent space. Clustering accuracy was shown in evaluation matrices between cluster assignments predicted by K-means and the reference cell types. The blue colorbar refers to the number of cells; (a) UMAP visualization of the extracted features from NMF with 128 latent features; (b) Evaluation matrices with 128 latent features.

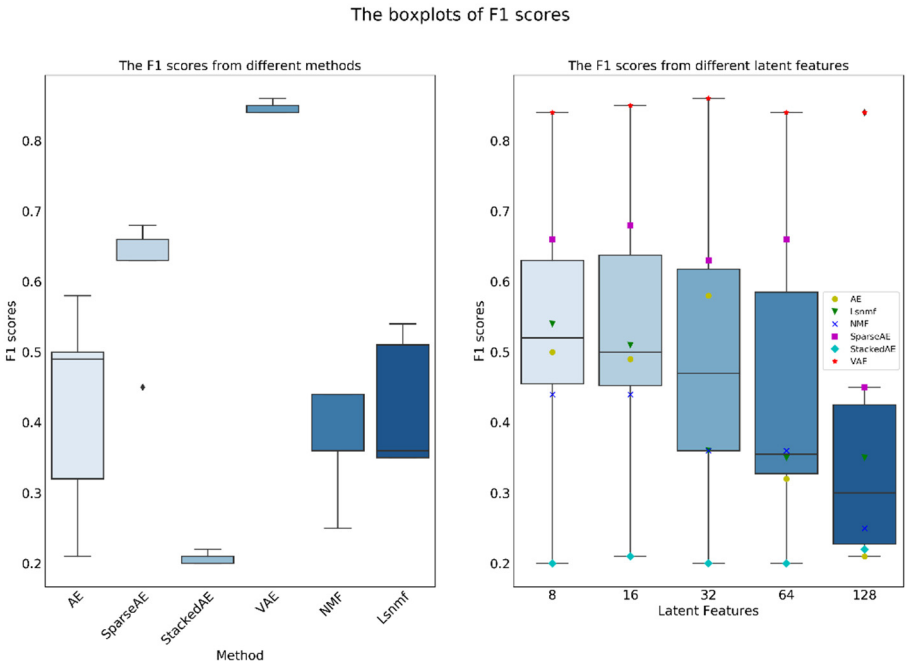

Figure S31. The boxplots of F1 scores generated from different methods and latent features.

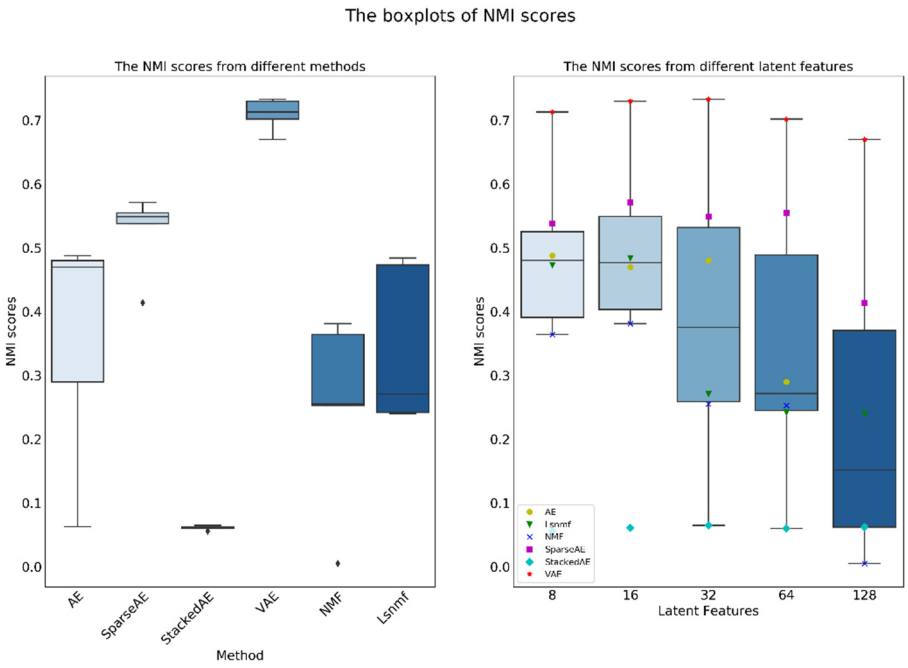

Figure S32. The boxplots of NMI scores generated from different methods and latent features.

Table S1. The clustering performance using General autoencoder with different dimension of latent features.

Latent feature dimension	F1 score	ARI	NMI	Silhouette_score
8	0.500	0.353	0.488	0.249
16	0.490	0.352	0.470	0.238
32	0.580	0.387	0.480	0.076
64	0.320	0.140	0.290	0.111
128	0.210	0.017	0.063	0.357

Table S2. The clustering performance using SparseAE with different dimension of latent features.

Latent feature dimension	F1 score	ARI	NMI	Silhouette_score
8	0.660	0.391	0.538	0.162
16	0.680	0.473	0.571	0.111
32	0.630	0.453	0.549	0.061
64	0.660	0.452	0.555	0.025
128	0.450	0.277	0.414	0.069

Table S3. The clustering performance using StackedAE with different dimension of latent features.

Latent feature dimension	F1 score	ARI	NMI	Silhouette_score
8	0.200	0.020	0.056	0.340
16	0.210	0.021	0.061	0.134
32	0.200	0.021	0.065	0.087
64	0.200	0.019	0.060	0.051
128	0.220	0.020	0.062	0.023

Table S4. The clustering performance using VAE with different dimension of latent features.

Latent feature dimension	F1 score	ARI	NMI	Silhouette_score
8	0.840	0.657	0.713	0.260
16	0.850	0.677	0.730	0.152
32	0.860	0.686	0.733	0.078
64	0.840	0.643	0.702	0.058
128	0.840	0.643	0.670	0.030

Table S5. The clustering performance using Lsnmf with different dimension of latent features.

Latent feature dimension	F1 score	ARI	NMI	Silhouette_score
8	0.540	0.302	0.473	0.288
16	0.510	0.283	0.484	0.210
32	0.360	0.092	0.271	0.084
64	0.350	0.077	0.242	0.065
128	0.350	0.076	0.240	0.035

Table S6. The clustering performance using NMF with different dimension of latent features.

Latent feature dimension	F1 score	ARI	NMI	Silhouette_score
8	0.440	0.154	0.364	0.364
16	0.440	0.133	0.381	0.345
32	0.360	0.082	0.255	0.202
64	0.360	0.082	0.253	0.084
128	0.250	0.001	0.005	0.821