Introduction

While every human genome is over 99% identical, the small fraction that differs holds insights into our ancestry. One informative type of variation is the single nucleotide polymorphism, which is a single-letter change in the DNA sequence that varies across individuals. Because they are passed through generations, SNPs reveal patterns of similarity and divergence between populations.

This project uses SNP data from the 1000 Genomes Project, an international effort to catalog human genetic variation. Although the dataset includes population labels, this analysis focuses on evaluating unsupervised models by removing those labels. The goal is to explore how well individuals group based on genetic similarity. By analyzing SNPs from chromosome 22, I aim to uncover population structure without relying on geographic labels.

Using dimensionality reduction and clustering, this project determines whether genetic data alone can recover known population groupings. In doing so, it demonstrates if unsupervised techniques are useful for this task.

Data Source

This project uses genotype data from the 1000 Genomes Project, focusing on chromosome 22. Chromosome 22 was selected due to its manageable size and high variant density, making it a practical starting point for exploratory analysis. With over 1 million SNPs in this dataset, it offers sufficient genetic diversity to capture meaningful population structure without the computational load of processing the entire genome. The data includes SNPs for 2,504 individuals from 26 populations, which are further grouped into five major superpopulations:

- AFR (African)
- EUR (European)
- EAS (East Asian)
- SAS (South Asian)
- AMR (Admixed American)

The raw dataset contains over 1.1 million SNPs across the 2,504 individuals, forming a matrix shape (2504, 1103547). Each SNP is type int8, representing biallelic genotype calls (0, 1, or 2 representing the number of alternate alleles).

Problem Statement

The goal is to cluster individuals into genetically similar groups using SNP data, without access to their population labels during training. This project explores whether unsupervised learning can uncover population structure from genetic data alone. This kind of analysis is useful in fields like disease research and forensic science.

Exploratory Data Analysis Procedure

To prepare the data for clustering, I first analyzed its structure. The dataset included 2,504 individuals and more than 1.1 million SNPs from chromosome 22, encoded as integer genotypes: 0 (homozygous reference), 1 (heterozygous), or 2 (homozygous alternate), representing the number of alternate alleles at each DNA site. As expected for genetic data, the dataset was very sparse, with many SNPs showing little to no variation across individuals.

Since genotype values were bounded (0, 1, 2), normalization was not necessary. Moreover, the preprocessed data did not contain any missing values, and outlier removal was not needed, as all values represented valid genotypes.

To reduce dimensionality, I selected the 10,000 SNPs with the highest variance across individuals. This maintained useful variation while reducing noise and making the dataset a manageable size.

Next, I applied PCA to further reduce dimensionality and visualize the underlying structure of the data. Plotting the first few principal components showed clear population divides and provided a low-dimensional representation suitable for clustering methods like K-Means. I also created a scree plot to show the variance explained by the first six components. Since the explained variance leveled off after the third component, I selected the top three to capture the most meaningful variation in the data.

At this stage, the data was prepared for unsupervised learning.

Model Building and Evaluation

I evaluated clustering performance using three metrics: Adjusted Rand Index (ARI), Normalized Mutual Information (NMI), and Purity Score. ARI measures how well the predicted clusters align with the true labels, adjusting for chance—where 1 represents perfect agreement and 0 suggests random grouping. NMI captures how much information is shared between the predicted and true labels, while Purity reflects how consistently each cluster contains members of a single true category. For all three metrics, higher values indicate better model performance.

As a baseline, I implemented a random clustering model that assigned each individual to one of 26 clusters (matching the number of known populations) without using genetic information. As expected, this random model captured no relationship between genotype and population labels, indicated by the low ARI, NMI, and purity. This null model serves as a reference for evaluating whether more sophisticated clustering methods produce results that go beyond random chance.

Next, I applied K-means clustering to the PCA-reduced data. I chose K-means because it is easy to interpret and efficient for high-dimensional datasets. Using k=26 to match the known populations produced weak results (purity= 0.202), suggesting the model struggled to distinguish between the 26 groups. An elbow curve analysis indicated k=5 as the best choice, likely reflecting the dataset's five superpopulations (AFR, EUR, EAS, SAS, AMR). Based on this, I re-evaluated K-means clustering (with k = 5) against superpopulation labels. This shift led to a significant boost in performance, achieving a purity of 0.9081, confirming that K-means is capturing broad genetic patterns in the data.

A confusion matrix showed that most misclassifications occurred within the Admixed American group, which was frequently split between its own cluster and the European group. Interestingly, the reverse was not true. The asymmetry is likely due to colonial-era gene flow, where EUR ancestry entered AMR populations, but not vice versa. Side-by-side scatter plots show the four well-separated superpopulations, with considerable overlap between the AMR and EUR groups, supporting these findings.

To complement K-means, I implemented agglomerative clustering as a second unsupervised approach. An initial model using ward linkage resulted in performance similar to those of K-means. To improve the results, I tested different combinations of linkage methods and distance metrics. The best-performing setup, average linkage with Euclidean distance, resulted in small gains in ARI, NMI, and purity, but still did not outperform K-means. The confusion matrix mirrored K-means results, notably misclassifying many AMR individuals as EUR. I finally tested whether agglomerative clustering could capture more fine-grained population structure by looping up to 26 clusters to match the known subpopulations. However, performance was low across all metrics, suggesting that the method struggled to distinguish closely related groups.

Results Summary Table

Model	ARI	NMI	Purity
K-Means (k=5)	0.8343	0.8544	0.9081
Agglomerative (avg, euclidean)	0.8350	0.8573	0.9050
Random Clustering	0.1912	0.5070	0.3027

Conclusion

This project demonstrated that unsupervised learning methods can detect genetic patterns using only SNP data, without relying on population labels. By analyzing over 1 million SNPs from chromosome 22 across 2,504 individuals in the 1000 Genomes Project, I assessed whether clustering algorithms could recover known populations based solely on genomic similarity.

Dimensionality reduction through PCA revealed clear structure in the data and provided a low-dimensional basis for clustering. K-means, when evaluated at the superpopulation level, showed strong performance across all metrics, demonstrating that it captured continental-level divisions encoded in the SNP data. Agglomerative clustering, using average linkage and Euclidean distance, performed similarly but did not surpass K-means. Both models struggled to uncover subpopulation structure, particularly among the Admixed American group.

These results affirm that unsupervised models can distinguish large-scale population structure. They also highlight the limitations of clustering for resolving more nuanced ancestry patterns, which may require supervised methods, more genomic data, or models that account for admixture. Overall, the project shows the potential of unsupervised learning in genomic research.

In [1]:
```
import numpy as np
import pandas as pd
import matplotlib.pyplot as plt
from sklearn.decomposition import PCA
from sklearn.preprocessing import StandardScaler
from sklearn.cluster import KMeans, AgglomerativeClustering
from sklearn.metrics import (
    adjusted_rand_score,
    normalized_mutual_info_score,
    confusion_matrix,
    ConfusionMatrixDisplay
)
from scipy.cluster.hierarchy import dendrogram, linkage
from matplotlib.cm import get_cmap
from matplotlib.colors import ListedColormap
from matplotlib.patches import Patch
from IPython.display import display
from collections import Counter
import allel
```

In [2]:
```
# Load data
callset = allel.read_vcf('../data/raw/ALL.chr22.phase3_shapeit2_mvncall_inte
                         fields=['samples', 'calldata/GT'],
                         alt_number=1)
```

In [3]:
```
# Extract genotype array
gt = callset['calldata/GT']

# Convert to diploid codes: 0 (hom ref), 1 (het), 2 (hom alt)
geno = allel.GenotypeArray(gt).to_n_alt().T

# Count missing values
missing_count = np.sum(geno < 0)
print(f"Total missing genotypes: {missing_count}")

# Convert to dataframe
df_geno = pd.DataFrame(geno)
```

```
Total missing genotypes: 0
```

In [4]:
```
df_geno.shape
```

Out[4]:
```
(2504, 1103547)
```

In [5]:
```
df_geno.head(10)
```

Out[5]:

	0	1	2	3	4	5	6	7	8	9	...	1103537	1103538	1103539	1103540	110354
0	0	0	0	0	0	0	0	0	0	1	...	0	0	0	0	(
1	0	0	0	0	0	0	0	0	0	0	...	0	0	0	0	(
2	0	0	0	0	0	0	0	0	0	0	...	0	0	0	0	(
3	0	0	0	0	0	0	0	0	0	0	...	0	0	0	0	(
4	0	0	0	0	0	0	0	0	0	0	...	0	0	0	0	(
5	0	0	0	0	0	0	0	0	0	0	...	0	0	0	0	(
6	0	0	0	0	0	0	0	0	0	1	...	0	0	0	0	(
7	0	0	0	0	0	0	0	0	0	0	...	0	0	0	0	(
8	0	0	0	0	0	0	0	0	0	0	...	0	0	0	0	(
9	0	0	0	0	0	0	0	0	0	1	...	0	0	0	0	(

10 rows × 1103547 columns

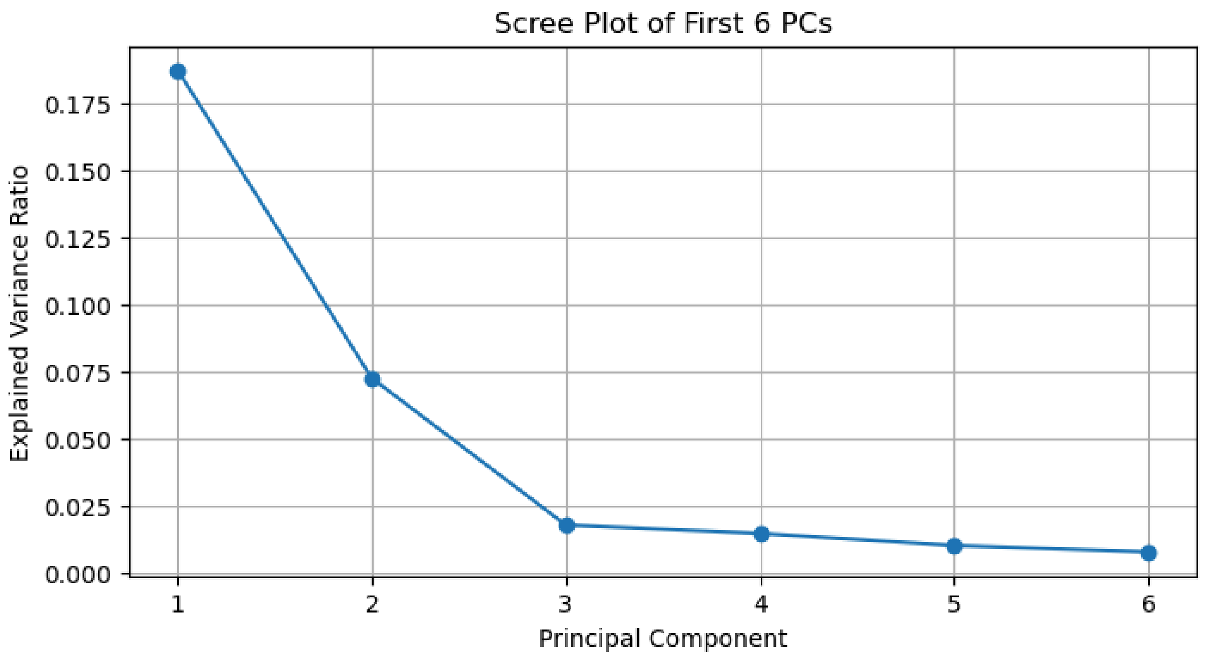
In [6]:
```
df_geno.info()
```
```
<class 'pandas.core.frame.DataFrame'>
RangeIndex: 2504 entries, 0 to 2503
Columns: 1103547 entries, 0 to 1103546
dtypes: int8(1103547)
memory usage: 2.6 GB
```

In [7]:
```
# Compute variance for each SNP
snp_variances = df_geno.var(axis=0)

# Select top 10,000 most variable SNPs
top_snps = snp_variances.nlargest(10000).index

# Subset the genotype matrix to those top SNPs
df_geno_top = df_geno[top_snps]

# Standardize the matrix pre PCA
scaler = StandardScaler()
X_std = scaler.fit_transform(df_geno_top)
```

In [8]:
```
# Run PCA
pca = PCA(n_components=6)
X_pca = pca.fit_transform(X_std)

# Print explained variance
explained = pca.explained_variance_ratio_
print(f"Explained variance by PC1: {explained[0]}")
print(f"Explained variance by PC2: {explained[1]}")
print(f"Explained variance by PC3: {explained[2]}")
print(f"Explained variance by PC4: {explained[3]}")
print(f"Explained variance by PC5: {explained[4]}")
print(f"Explained variance by PC6: {explained[5]}")
```

```
cumulative_variance = np.cumsum(pca.explained_variance_ratio_)
print(f"Cumulative variance: {cumulative_variance}")


# Plot explained variance by principal comp
plt.figure(figsize=(8, 4))
plt.plot(
    np.arange(1, 7),  # x: components 1 to 6
    pca.explained_variance_ratio_,  # y: their variance
    marker='o'
)
plt.xlabel('Principal Component')
plt.ylabel('Explained Variance Ratio')
plt.title('Scree Plot of First 6 PCs')
plt.grid(True)
plt.xticks(np.arange(1, 7))
plt.show()
```

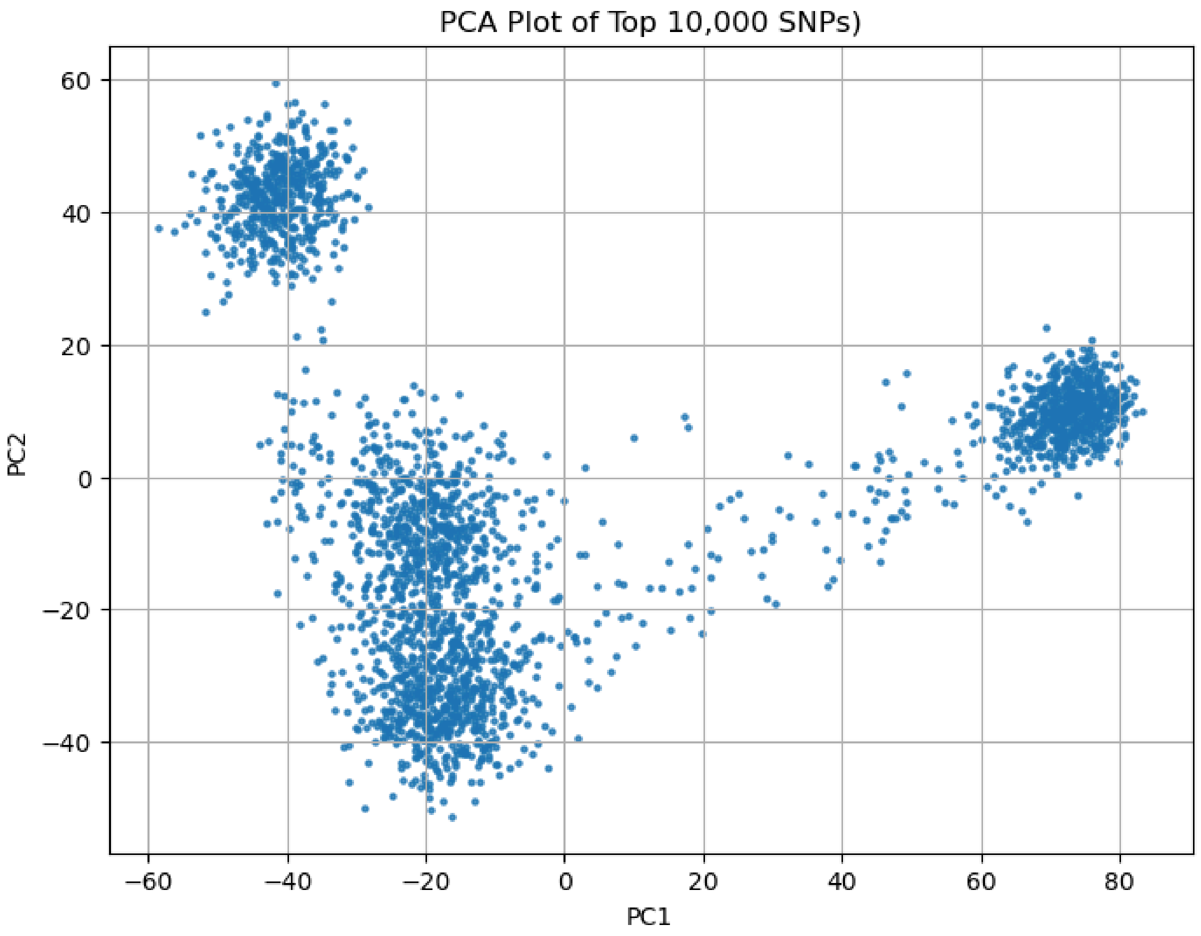
```
Explained variance by PC1: 0.1875949502054576
Explained variance by PC2: 0.0726913992404625
Explained variance by PC3: 0.01790026368218306
Explained variance by PC4: 0.014759035934174096
Explained variance by PC5: 0.01026593184076825
Explained variance by PC6: 0.007912127308167191
Cumulative variance: [0.18759495 0.26028635 0.27818661 0.29294565 0.30321158
0.31112371]
```



Scree plot showing the variance explained by the first six principal components from PCA. The explained variance begins to level off after the third component, so I will use three principal components to capture the most meaningful variance in the data.

In [9]:
```
# Re-run PCA with optimized number of components: 3
pca = PCA(n_components=3)
X_pca = pca.fit_transform(X_std)
```

In [10]:
```
# Plot the first 2 principal components
plt.figure(figsize=(8,6))
plt.scatter(X_pca[:, 0], X_pca[:, 1], s=5, alpha=0.8)
plt.xlabel('PC1')
plt.ylabel('PC2')
plt.title('PCA Plot of Top 10,000 SNPs)')
plt.grid(True)
plt.show()
```



A 2D scatter plot; From the plot, you observe several distinct groupings, indicating that PCA successfully captured population structure in the genetic data.

In [11]:
```
# Load the metadata
sample_info = pd.read_csv("../data/raw/20130606_g1k.ped.txt", sep="\t")

print(sample_info.columns.tolist())

# Preview the data
sample_info.head()
```

```
['Family ID', 'Individual ID', 'Paternal ID', 'Maternal ID', 'Gender', 'Phen
otype', 'Population', 'Relationship', 'Siblings', 'Second Order', 'Third Ord
er', 'Other Comments']
```

Out[11]:

	Family ID	Individual ID	Paternal ID	Maternal ID	Gender	Phenotype	Population	Relationshi
0	BB01	HG01879	0	0	1	0	ACB	fathe
1	BB01	HG01880	0	0	2	0	ACB	mothe
2	BB01	HG01881	HG01879	HG01880	2	0	ACB	chil
3	BB02	HG01882	0	0	1	0	ACB	fathe
4	BB02	HG01883	0	0	2	0	ACB	mothe

In [12]:

```
# Convert VCF sample IDs to DataFrame
sample_ids = pd.Series(callset['samples'], name='Individual ID')

# Merge with population labels
true_label_merge = pd.merge(sample_ids.to_frame(), sample_info, on='Individu

# Check for missing population labels
missing = true_label_merge['Population'].isna().sum()
print(f"Samples with missing population label: {missing}")
```

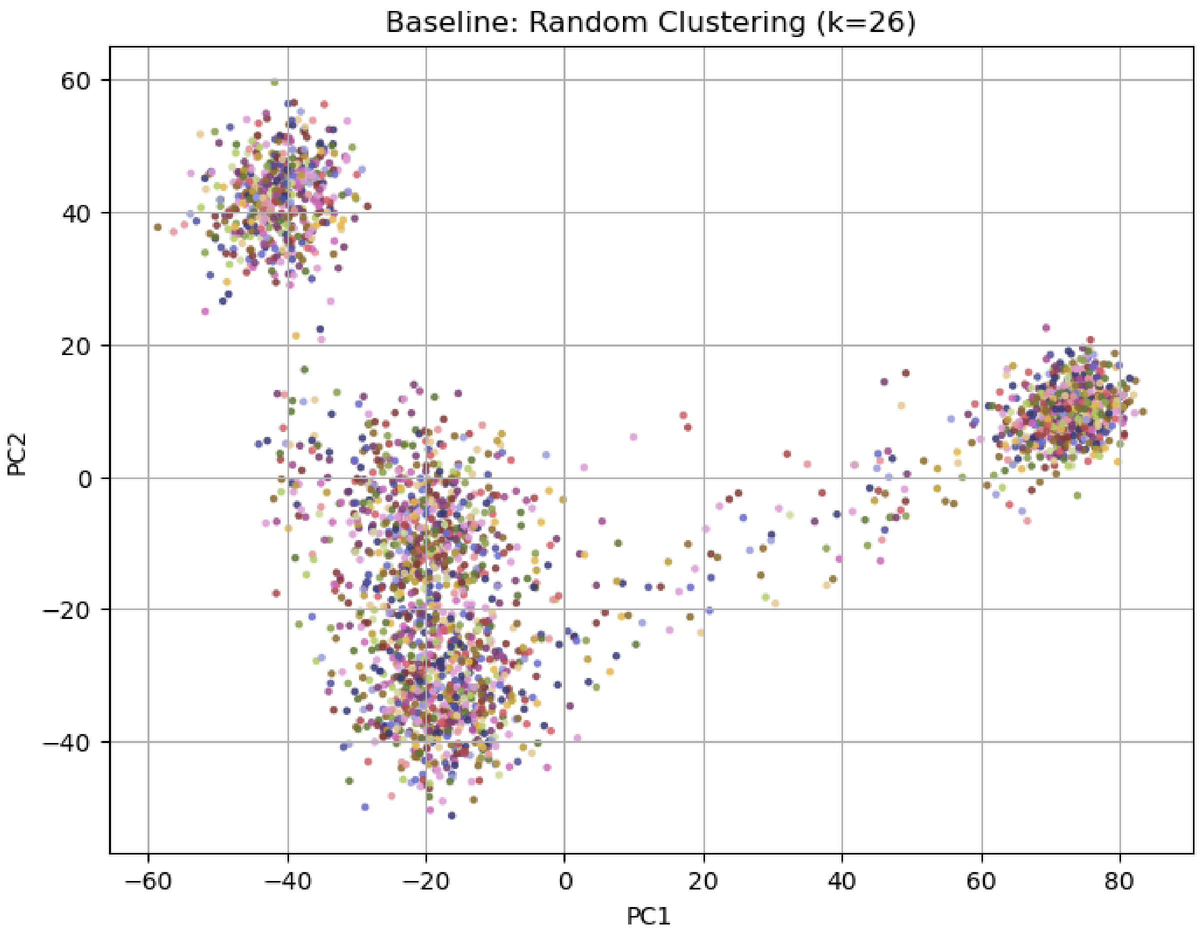
```
Samples with missing population label: 0
```

In [13]:

```
true_labels = true_label_merge['Population'].values
```

In [14]:

```
# Set number of clusters to 26 for the known 26 populations as defined by th
k = len(np.unique(true_labels))

# Create random cluster labels
np.random.seed(42)
random_labels = np.random.randint(0, k, size=X_pca.shape[0])

# Get a base colormap and sample colors
base_cmap = plt.get_cmap('tab20b')
colors = base_cmap(np.linspace(0, 1, k))
custom_cmap = ListedColormap(colors)

# Plot random clusters in PCA space
plt.figure(figsize=(8, 6))
plt.scatter(
    X_pca[:, 0], X_pca[:, 1],
    c=random_labels,
    cmap=custom_cmap,
    s=5,
    alpha=0.8
)
plt.xlabel('PC1')
plt.ylabel('PC2')
plt.title(f'Baseline: Random Clustering (k={k})')
plt.grid(True)
plt.show()
```



This code generates a random clustering baseline in 2-D PCA space. It serves as a visual reference for evaluating whether other clustering methods reveal patterns beyond chance.

```
In [15]: def purity_score(y_true, y_pred):
             # Create a contingency matrix
             contingency_matrix = pd.crosstab(y_true, y_pred)
             # Purity is the sum of the largest count in each predicted cluster
             return np.sum(np.amax(contingency_matrix.values, axis=0)) / np.sum(conti

         # Evaluate ARI and NMI
         ari = adjusted_rand_score(true_labels, random_labels)
         nmi = normalized_mutual_info_score(true_labels, random_labels)
         purity = purity_score(true_labels, random_labels)

         # Print all metrics
         print("Random Clustering Performance\n")
         print(f"Adjusted Rand Index: {ari}")
         print(f"Normalized Mutual Information: {nmi}")
         print(f"Purity Score: {purity}")
```

```
Random Clustering Performance

Adjusted Rand Index: 0.00017068813623577787
Normalized Mutual Information: 0.042342145052493056
Purity Score: 0.08266773162939298
```

This code evaluates the performance of a baseline model using random clustering. It serves as a numerical reference to determine whether other clustering methods offer meaningful improvements.

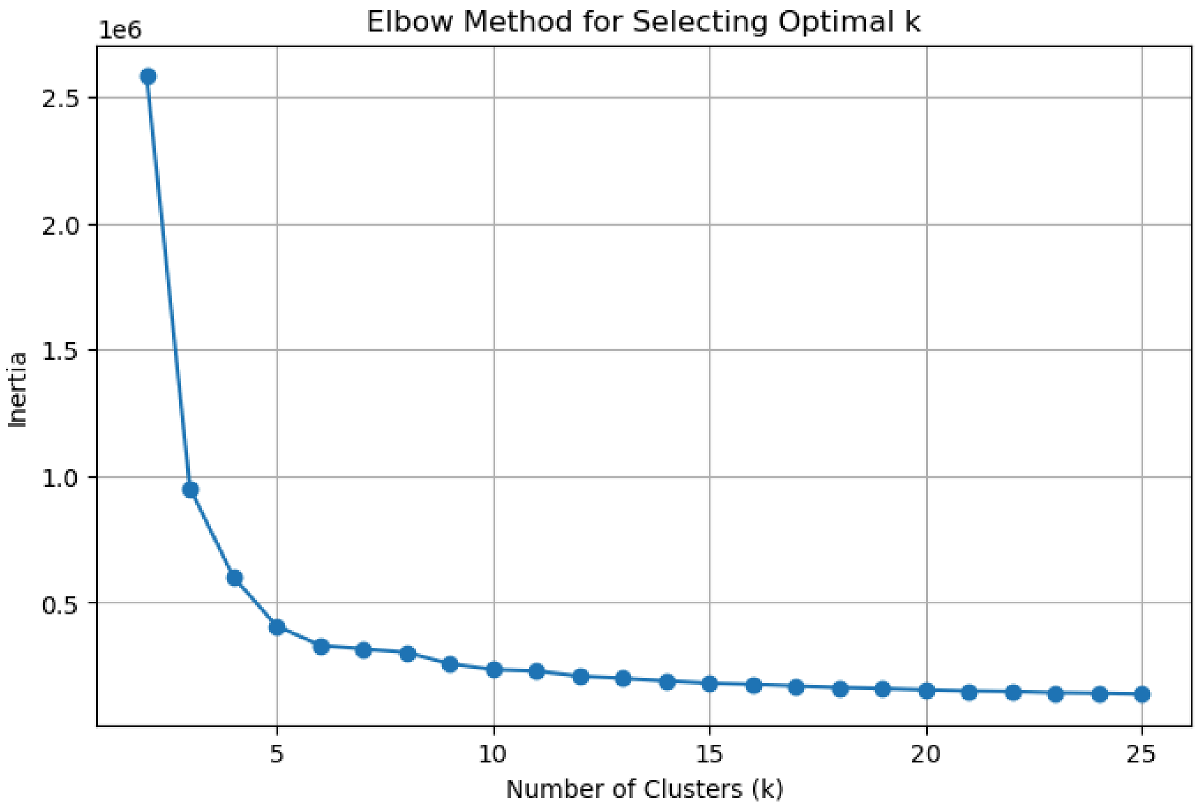
In [16]:
```
# Define purity function
def purity_score(y_true, y_pred):
    contingency_matrix = pd.crosstab(y_true, y_pred)
    return np.sum(np.amax(contingency_matrix.values, axis=0)) / np.sum(conti
```

In [17]:
```
# Define number of clusters to match number of unique populations
k = len(np.unique(true_labels))

# Run k-means
kmeans = KMeans(n_clusters=k, random_state=42)
kmeans_labels = kmeans.fit_predict(X_pca)

# Evaluate clustering performance
ari = adjusted_rand_score(true_labels, kmeans_labels)
nmi = normalized_mutual_info_score(true_labels, kmeans_labels)
purity = purity_score(true_labels, kmeans_labels)

# Print results
print(f"K-Means Clustering Performance (k={k})\n")
print(f"Adjusted Rand Index: {ari}")
print(f"Normalized Mutual Information: {nmi}")
print(f"Purity Score: {purity}")
```

```
K-Means Clustering Performance (k=26)

Adjusted Rand Index: 0.19075306750425727
Normalized Mutual Information: 0.5068878806132646
Purity Score: 0.3055111821086262
```

Compared to the random baseline, K-means achieved higher ARI, NMI, and Purity. However, the scores are still relatively low, indicating that K-means only partially recovered the underlying population structure and may not be the most effective method for this task.

In [18]:
```
# Range of k values to test
k_max = len(np.unique(true_labels))
ks = range(2, k_max)
inertias = []

# Fit KMeans for each k and store inertia
for k in ks:
    kmeans = KMeans(n_clusters=k, random_state=42)
    kmeans.fit(X_pca)
    inertias.append(kmeans.inertia_)

# Plot the elbow curve
plt.figure(figsize=(8, 5))
plt.plot(ks, inertias, marker='o')
plt.xlabel('Number of Clusters (k)')
plt.ylabel('Inertia')
plt.title('Elbow Method for Selecting Optimal k')
plt.grid(True)
plt.show()

# Also print numerical values in a table
elbow_df = pd.DataFrame({'k': ks, 'inertia': inertias})
print(elbow_df)
```



```
     k       inertia
0    2  2.583625e+06
1    3  9.538378e+05
2    4  6.027417e+05
3    5  4.081652e+05
4    6  3.312923e+05
5    7  3.172749e+05
6    8  3.034709e+05
7    9  2.580140e+05
8   10  2.351764e+05
9   11  2.295039e+05
10  12  2.093945e+05
11  13  2.007959e+05
12  14  1.909493e+05
13  15  1.816427e+05
14  16  1.768268e+05
15  17  1.706767e+05
16  18  1.641988e+05
17  19  1.602591e+05
18  20  1.551964e+05
19  21  1.505392e+05
20  22  1.479358e+05
21  23  1.435209e+05
22  24  1.416940e+05
23  25  1.385208e+05
```

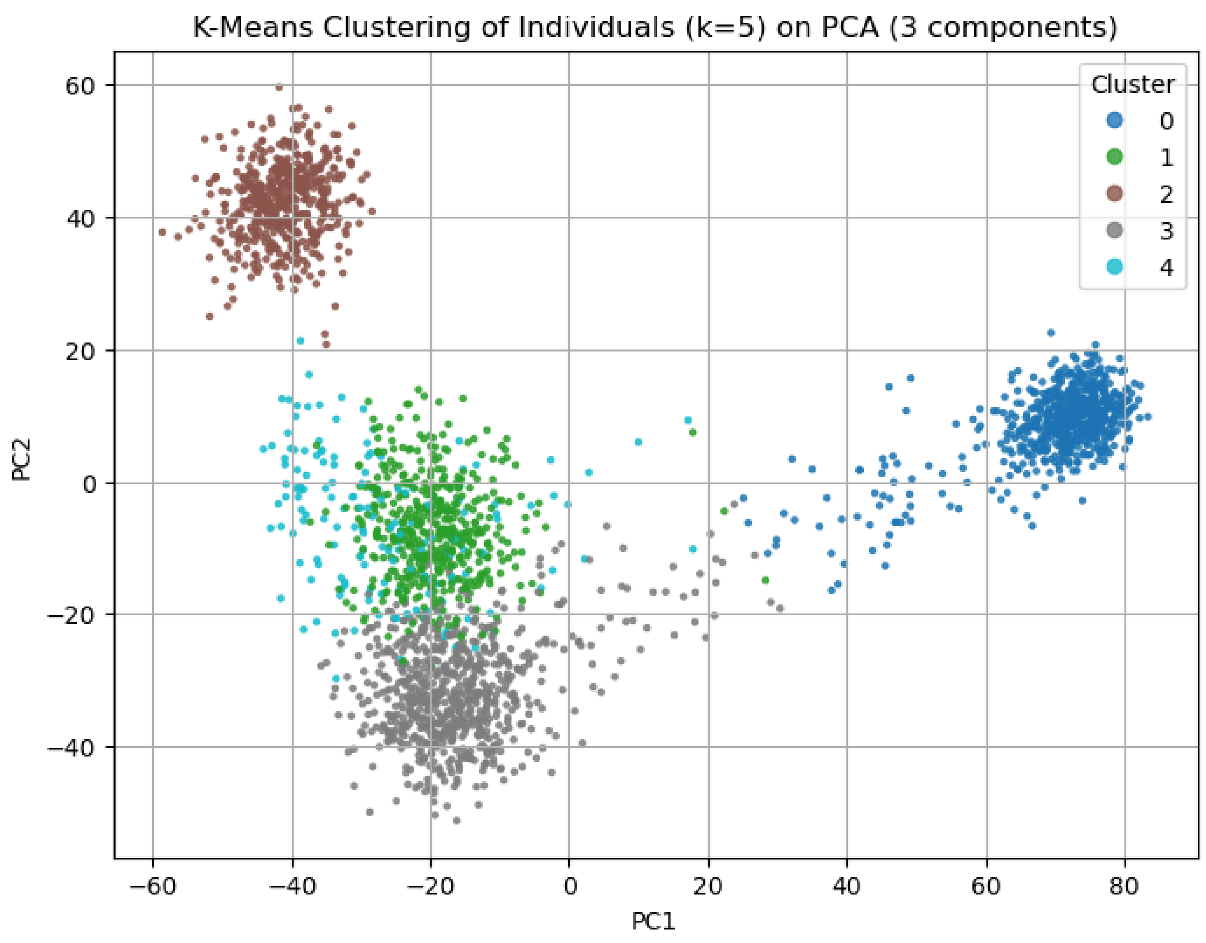
This code uses the elbow method to find the optimal number of clusters for K-means. It fits models for a range of k values (2 to 26), notes the inertia (within-cluster variance), and plots the results. The "elbow" in the curve indicates where adding more clusters has diminishing returns. Based on the plot, k=5 is the best choice—likely because the model is capturing the structure of the five major superpopulations present in the dataset (AFR:African, EUR:European, EAS:East Asian, SAS:South Asian, AMR:Admixed American)

In [19]:
```python
# Set k to 5 based on elbow plot
k = 5

# Run k-means
kmeans = KMeans(n_clusters=k, random_state=42)
kmeans_labels = kmeans.fit_predict(X_pca)

# Evaluate clustering
ari = adjusted_rand_score(true_labels, kmeans_labels)
nmi = normalized_mutual_info_score(true_labels, kmeans_labels)
purity = purity_score(true_labels, kmeans_labels)

# Print results
print(f"K-Means Clustering Performance(k={k})\n")
print(f"Adjusted Rand Index: {ari}")
print(f"Normalized Mutual Information: {nmi}")
print(f"Purity Score: {purity}")
```

```
K-Means Clustering Performance(k=5)

Adjusted Rand Index: 0.2182359020556783
Normalized Mutual Information: 0.5831835563773446
Purity Score: 0.20287539936102236
```

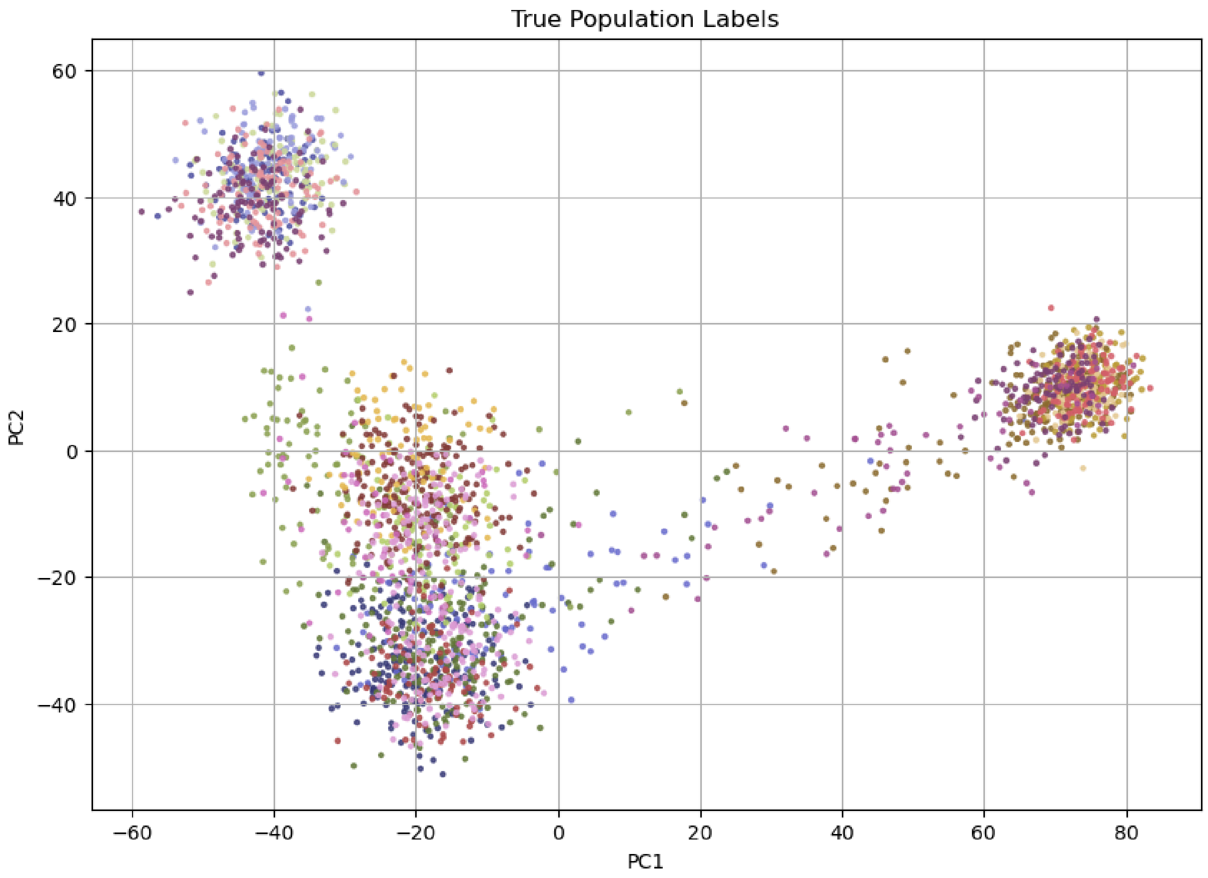
K-means clustering with k=5 outperformed k=26 on both ARI and NMI, indicating better alignment with the true population structure. Although k=26 yielded a higher purity score, this likely reflects over-fragmentation rather than meaningful clusters. Despite its relative improvement, the low performance of k=5 suggests that k-means may not be well-suited for this task.

In [20]:
```
# Visualize the results of K-means clustering (k=5) in 2-D PCA space
plt.figure(figsize=(8, 6))
scatter = plt.scatter(
    X_pca[:, 0], X_pca[:, 1],
    c=kmeans_labels,
    cmap='tab10',
    s=5,
    alpha=0.8
)

plt.xlabel('PC1')
plt.ylabel('PC2')
plt.title('K-Means Clustering of Individuals (k=5) on PCA (3 components)')
plt.grid(True)
plt.legend(*scatter.legend_elements(), title="Cluster")
plt.show()
```



K-Means Clustering Visualization; This plot uses K-means clustering with k=5 on data reduced to 3 principal components, but only the first 2 components are plotted, creating a 2-D visualization. From the plot, we can see that K-means clustering resulted in distinct clusters. However, some overlap and spread among the clusters indicate that the separation is not perfect, and finer population distinctions may not be well captured with these parameters.

In [21]:
```
# Factorize true labels
true_labels_int = pd.factorize(true_labels)[0]

# Set number of unique populations
k = len(np.unique(true_labels_int))

# Create custom colormap (same as baseline)
base_cmap = plt.get_cmap('tab20b')
colors = base_cmap(np.linspace(0, 1, k))
custom_cmap = ListedColormap(colors)

# Plot true population labels
plt.figure(figsize=(10, 7))
scatter = plt.scatter(
    X_pca[:, 0], X_pca[:, 1],
    c=true_labels_int,
    cmap=custom_cmap,
    s=5,
    alpha=0.8
)

plt.xlabel('PC1')
plt.ylabel('PC2')
plt.title('True Population Labels')
plt.grid(True)
plt.show()
```



The plot shows the true population labels for individuals projected into 2D PCA space.The 26 populations overlap significantly, making them difficult to distinguish. In contrast, broader patterns suggest that individuals from the same continent—at a less granular scale—may cluster together. CCollapsing the 26 populations into the 5 superpopulations defined by the 1000 Genomes Project helps align the number of clusters (k=5) with the broader genetic structure that K-means is more likely to detect.

In [22]:
```
# Dictionary to map population codes to superpopulations
pop_to_superpop = {
    # AFR
    'YRI': 'AFR', 'LWK': 'AFR', 'GWD': 'AFR', 'MSL': 'AFR', 'ESN': 'AFR', 'A
    # EUR
    'CEU': 'EUR', 'TSI': 'EUR', 'FIN': 'EUR', 'GBR': 'EUR', 'IBS': 'EUR',
    # EAS
    'CHB': 'EAS', 'JPT': 'EAS', 'CHS': 'EAS', 'CDX': 'EAS', 'KHV': 'EAS',
    # SAS
    'GIH': 'SAS', 'PJL': 'SAS', 'BEB': 'SAS', 'STU': 'SAS', 'ITU': 'SAS',
    # AMR
    'MXL': 'AMR', 'PUR': 'AMR', 'CLM': 'AMR', 'PEL': 'AMR'
}
```

In [23]:
```
# Map population codes to superpopulations
superpop_labels = true_label_merge['Population'].map(pop_to_superpop)

# Check for any unmatched codes
unmatched = superpop_labels.isna().sum()
print(f"Unmatched population codes: {unmatched}")
```

```
Unmatched population codes: 0
```

In [24]:
```
# Recalculate metrics for kmeans_labels vs. superpop_labels
ari = adjusted_rand_score(superpop_labels, kmeans_labels)
nmi = normalized_mutual_info_score(superpop_labels, kmeans_labels)
purity = purity_score(superpop_labels, kmeans_labels)

print("\nK-Means Clustering (k=5) — Evaluated Against Superpopulations\n")
print(f"Adjusted Rand Index: {ari}")
print(f"Normalized Mutual Information: {nmi}")
print(f"Purity Score: {purity}")
```

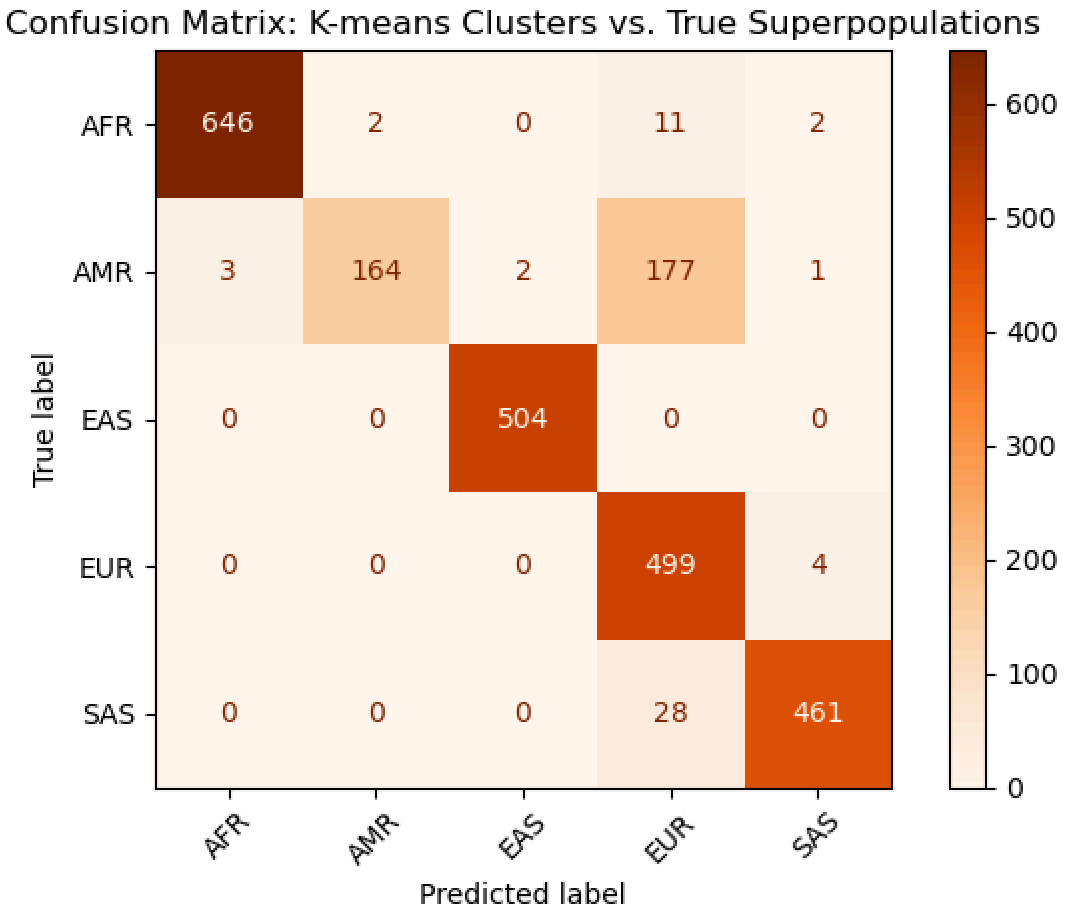
```
K-Means Clustering (k=5) — Evaluated Against Superpopulations

Adjusted Rand Index: 0.8342646178162892
Normalized Mutual Information: 0.8543751102584954
Purity Score: 0.90814696485623
```

This three code blocks above maps the 26 granular population labels to 5 broader superpopulations (AFR, EUR, EAS, SAS, AMR). It then re-evaluates the existing K-means clustering results (k=5) by comparing them to these superpopulation labels instead of the original 26 groups. This helps determine whether K-means captured the broader continental-level structure more accurately like we hypothesized.

Based on the high values for ARI, NMI, and Purity, K-means clustering is highly effective at capturing broad genetic patterns in the dataset. While it struggled to distinguish fine-grained population differences, it aligns closely with the continental-level groupings represented by the superpopulations.

In [25]:
```
# Match clusters to superpopulation label
cluster_df = pd.DataFrame({
    'cluster': kmeans_labels,
    'superpop': superpop_labels
})

# Create mapping from cluster to dominant superpop
cluster_to_superpop = (
    cluster_df.groupby('cluster')['superpop']
    .agg(lambda x: x.value_counts().idxmax())
    .to_dict()
)

# Map each cluster label to the correct dominant superpopulation
predicted_superpops = [cluster_to_superpop[cluster] for cluster in kmeans_la
```

```
superpop_order = ['AFR', 'AMR', 'EAS', 'EUR', 'SAS']

# Compute confusion matrix
cm = confusion_matrix(superpop_labels, predicted_superpops, labels=superpop_

# Confusion matrix
disp = ConfusionMatrixDisplay(confusion_matrix=cm, display_labels=superpop_c
disp.plot(cmap="Oranges", xticks_rotation=45)
plt.title("Confusion Matrix: K-means Clusters vs. True Superpopulations")
plt.tight_layout()
plt.show()
```

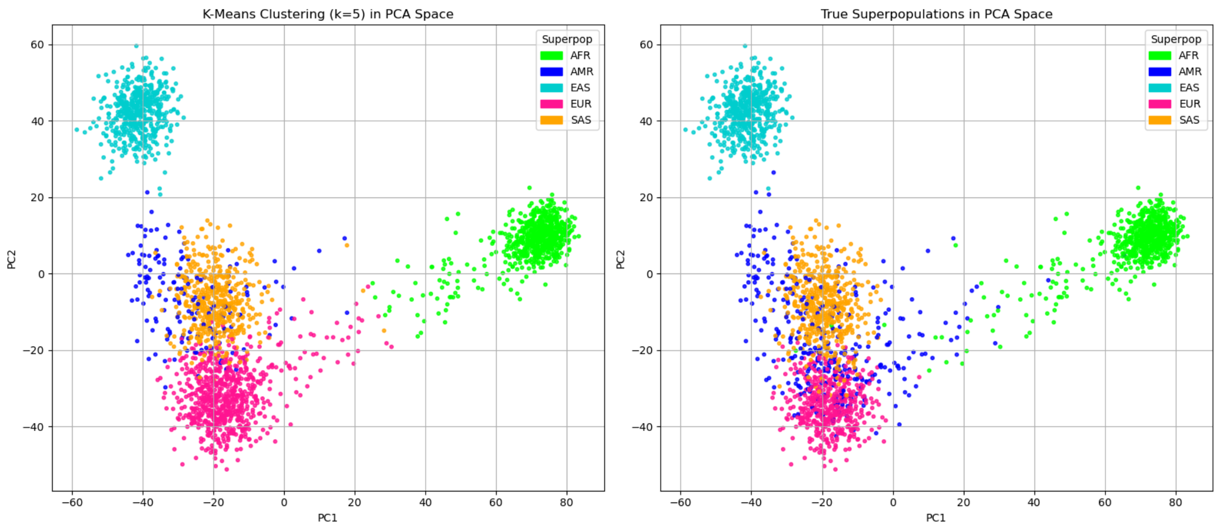


The model demonstrates high overall accuracy, particularly for the AFR, EAS, EUR, and SAS populations. The main source of misclassification arises with the AMR population, which is split between its own cluster and the EUR group. This pattern suggests underlying genetic similarity between AMR and EUR populations.

Interestingly, the model recognize European features in AMR genomes and misclassifies them as EUR, while EUR individuals are not misclassified as AMR. This asymetrical misclassification likely reflects historically uneven genetic exchange: AMR populations (especially those from Central and South America) carry substantial European ancestry due to colonial-era admixture, whereas EUR populations lack reciprocal gene flow from the Americas.

```
In [26]: # Define color mapping
superpop_order = ['AFR', 'AMR', 'EAS', 'EUR', 'SAS']
color_palette = ['#00ff00', '#0000ff', '#00ced1', '#ff1493', '#ffa500']
superpop_to_color = dict(zip(superpop_order, color_palette))

# Map true superpopulation labels to color codes
superpop_labels_mapped = superpop_labels.map(superpop_to_color)

# Map K-means cluster labels to dominant superpopulations
cluster_df = pd.DataFrame({
    'cluster': kmeans_labels,
    'superpop': superpop_labels
})

cluster_to_superpop = (
    cluster_df.groupby('cluster')['superpop']
    .agg(lambda x: x.value_counts().idxmax())
    .to_dict()
)

cluster_colors = [superpop_to_color[cluster_to_superpop[c]] for c in kmeans_

# Legend
legend_handles = [
    Patch(color=superpop_to_color[pop], label=pop) for pop in superpop_order
]

# Side by side plot
fig, axes = plt.subplots(1, 2, figsize=(16, 7))

# K-means clustering
axes[0].scatter(
    X_pca[:, 0], X_pca[:, 1],
    c=cluster_colors,
    s=10,
    alpha=0.8
)
axes[0].set_title("K-Means Clustering (k=5) in PCA Space")
axes[0].set_xlabel("PC1")
axes[0].set_ylabel("PC2")
axes[0].grid(True)
axes[0].legend(handles=legend_handles, title="Superpop")

# True superpopulations
axes[1].scatter(
    X_pca[:, 0], X_pca[:, 1],
    c=superpop_labels_mapped,
    s=10,
    alpha=0.8
)
axes[1].set_title("True Superpopulations in PCA Space")
axes[1].set_xlabel("PC1")
axes[1].set_ylabel("PC2")
axes[1].grid(True)
axes[1].legend(handles=legend_handles, title="Superpop")
```

```
plt.tight_layout()
plt.show()
```



The left plot shows how K-means assigned clusters while the right panel shows the ground truth superpopulations. We see the AMR individuals (dark blue) are widely dispersed in both plots and frequently overlap with the EUR cluster (pink) in the left plot. The plot reinforces the confusion matrix by visually showing a key area of misclassification: many AMR individuals (dark blue) are incorrectly grouped with the EUR cluster (pink) in the K-means plot. This is evident when comparing corresponding points across the two plots.

In [27]:
```
# Agglomerative Clustering
k = 5
agglo = AgglomerativeClustering(n_clusters=k, linkage='ward')
agglo_labels = agglo.fit_predict(X_pca)

# Evaluate
ari = adjusted_rand_score(superpop_labels, agglo_labels)
nmi = normalized_mutual_info_score(superpop_labels, agglo_labels)
purity = purity_score(superpop_labels, agglo_labels)

print(f"Agglomerative Clustering (k={k})\n")
print(f"Adjusted Rand Index: {ari}")
print(f"Normalized Mutual Information: {nmi}")
print(f"Purity Score: {purity}")
```

```
Agglomerative Clustering (k=5)

Adjusted Rand Index: 0.7950083165614241
Normalized Mutual Information: 0.8190894157333964
Purity Score: 0.896964856230032
```

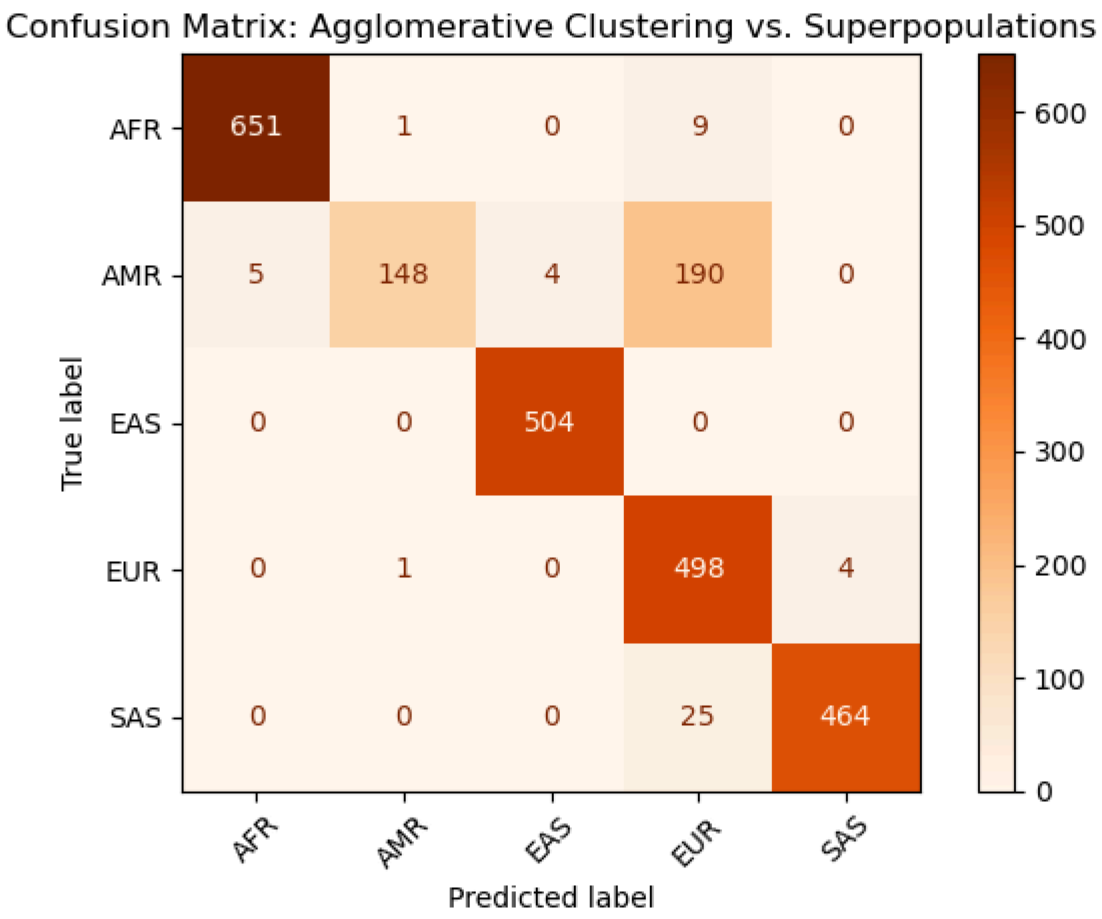
Agglomerative clustering held up well compared to K-means, achieving similar performance across all metrics. In the next steps, I will explore ways to fine-tune the agglomerative model to see if it can exceed K-means in accuracy.

In [28]:
```
# Define linkage methods and distance metrics
linkage_methods = ['ward', 'average', 'complete', 'single']
distance_metrics = ['euclidean', 'manhattan', 'cosine']

# Results
results = []

for linkage in linkage_methods:
    for metric in distance_metrics:
        # ward linkage can only have euclidean metric
        if linkage == 'ward' and metric != 'euclidean':
            continue
        try:
            model = AgglomerativeClustering(
                n_clusters=5,
                linkage=linkage,
                metric=metric
            )
            labels = model.fit_predict(X_pca)

            purity = purity_score(superpop_labels, labels)
            ari = adjusted_rand_score(superpop_labels, labels)
            nmi = normalized_mutual_info_score(superpop_labels, labels)

            results.append({
                'Linkage': linkage,
                'Metric': metric,
                'Purity': purity,
                'ARI': ari,
                'NMI': nmi
            })
        except Exception as e:
            results.append({
                'Linkage': linkage,
                'Metric': metric,
                'Purity': None,
                'ARI': None,
                'NMI': None,
                'Error': str(e)
            })

# Convert results to dataframe & sort
results_df = pd.DataFrame(results).sort_values(by='Purity', ascending=False)
print(results_df)
```

```
    Linkage     Metric    Purity       ARI       NMI
1   average  euclidean  0.904553  0.834790  0.856727
2   average  manhattan  0.900559  0.834880  0.859840
0      ward  euclidean  0.896965  0.795008  0.819089
3   average     cosine  0.887780  0.815112  0.843852
6  complete     cosine  0.859824  0.805654  0.838520
4  complete  euclidean  0.710863  0.599837  0.743612
5  complete  manhattan  0.707668  0.599317  0.733480
8    single  manhattan  0.466054  0.221283  0.475452
7    single  euclidean  0.465256  0.220738  0.475189
9    single     cosine  0.265176  0.000080  0.004104
```

I looped through different combinations of linkage methods and distance metrics for agglomerative clustering. The best-performing configuration was average linkage with euclidean distance. Although tuning improved the performance of the agglomerative model, it still did not surpass the results of K-means clustering.

In [29]:
```python
# Run agglomerative clustering with best parameters
best_model = AgglomerativeClustering(
    n_clusters=5,
    linkage='average',
    metric='euclidean'
)
best_labels = best_model.fit_predict(X_pca)

# Map cluster labels to superpopulations
cluster_df = pd.DataFrame({
    'cluster': best_labels,
    'superpop': superpop_labels
})
cluster_to_superpop = cluster_df.groupby('cluster')['superpop'].agg(lambda x
predicted_superpops = [cluster_to_superpop[cluster] for cluster in best_labe

# Confusion matrix
superpop_order = ['AFR', 'AMR', 'EAS', 'EUR', 'SAS']
cm = confusion_matrix(superpop_labels, predicted_superpops, labels=superpop_
disp = ConfusionMatrixDisplay(confusion_matrix=cm, display_labels=superpop_o
disp.plot(cmap="Oranges", xticks_rotation=45)
plt.title("Confusion Matrix: Agglomerative Clustering vs. Superpopulations")
plt.tight_layout()
plt.show()
```



This confusion matrix shows that, like K-means, the agglomerative clustering model frequently misclassified AMR individuals as EUR. This is most likely a result of genetic similarity due to admixture, making it difficult for the model to distinguish the two groups.

In [30]:
```
# Store results for each k
results = []

# Loop over number of clusters from 2 to 26
for k in range(2, 27):
    try:
        model = AgglomerativeClustering(n_clusters=k, linkage='average', met
        labels = model.fit_predict(X_pca)

        ari = adjusted_rand_score(true_labels, labels)
        nmi = normalized_mutual_info_score(true_labels, labels)
        purity = purity_score(true_labels, labels)

        results.append({
            'n_clusters': k,
            'ARI': ari,
            'NMI': nmi,
            'Purity': purity
        })
    except Exception as e:
        print(f"Failed for k={k}: {e}")
```

```
# Create a dataframe of results
results_df = pd.DataFrame(results)
print(results_df)
```

```
    n_clusters       ARI       NMI    Purity
0            2  0.048389  0.289540  0.087859
1            3  0.113525  0.460399  0.129792
2            4  0.136883  0.500362  0.160543
3            5  0.217374  0.583247  0.200879
4            6  0.223059  0.589397  0.211661
5            7  0.231384  0.593851  0.223243
6            8  0.231943  0.595389  0.224042
7            9  0.231953  0.595408  0.224840
8           10  0.230727  0.596154  0.233227
9           11  0.230556  0.595367  0.233227
10          12  0.230066  0.594119  0.233227
11          13  0.230075  0.594269  0.233626
12          14  0.230074  0.594359  0.233626
13          15  0.230046  0.594121  0.234026
14          16  0.229833  0.593510  0.234026
15          17  0.229572  0.593391  0.234824
16          18  0.228816  0.592055  0.237620
17          19  0.229066  0.590930  0.240016
18          20  0.228497  0.590327  0.240016
19          21  0.228869  0.590172  0.240815
20          22  0.228463  0.589693  0.240815
21          23  0.228464  0.589903  0.241214
22          24  0.228355  0.589740  0.241214
23          25  0.228357  0.590111  0.242013
24          26  0.238459  0.589160  0.251597
```

Here I wanted to test whether agglomerative clustering could capture fine-grained genetic structure by distinguishing all 26 populations, unlike K-means which performed best with 5 clusters. However, the results show that even as the number of clusters increased, the ARI, NMI, and Purity scores were low. This indicates that agglomerative clustering was not able to recover detailed population-level differences present in the dataset.

In [32]:
```
# Comparison dataframe
comparison_df = pd.DataFrame([

    {
        'Model': 'K-Means (k=5)',
        'ARI': 0.8343,
        'NMI': 0.8544,
        'Purity': 0.9081
    },
    {
        'Model': 'Agglomerative (avg, euclidean)',
        'ARI': 0.8350,
        'NMI': 0.8573,
        'Purity': 0.9050
    },
    {
        'Model': 'Random Clustering',
        'ARI': 0.1912,
        'NMI': 0.5070,
        'Purity': 0.3027
    },
])

print(comparison_df)
```

```
                            Model     ARI     NMI  Purity
0                    K-Means (k=5)  0.8343  0.8544  0.9081
1  Agglomerative (avg, euclidean)  0.8350  0.8573  0.9050
2                Random Clustering  0.1912  0.5070  0.3027
```