Supporting information

Tandem mass spectrometry imaging reveals distinct accumulation patterns of steroid structural isomers in human adrenal glands

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Abstract

Visualizing tissue distribution of steroid hormones is a promising application of MALDI mass spectrometry imaging (MSI). On-tissue chemical derivatization using Girard T reagent has enhanced the ionization efficiency of steroids. However, discriminating between structural isomers with distinct bioactivities remains a challenge. Herein, we used ion trap MS/tandem MS (MS^3) to distinguish a mineral corticoid aldosterone (Aldo) and a glucocorticoid cortisol (F), from their structural isomers. Our method is also useful to detect hybrid steroids (18-hydroxycortisol [18-OHF] and 18-oxocortisol) with sufficient signal-to-noise ratio. The clinical applicability of the tandem MS method was evaluated by analyzing F, Aldo, and 18-OHF distributions in human adrenal glands. In such clinical specimens, small Aldo-producing cell clusters (APCCs) were identified and were first found to produce a high level of Aldo and not to contain F. Moreover, a part of APCCs produced 18-OHF, presumably converted from F by APCC-specific CYP11B2 activity. Catecholamine species were also visualized with another derivatization reagent

(TAHS), and those profiling successfully discriminated pheochromocytoma species. These tandem MSI-methods, coupled with on-tissue chemical derivatization has proven to be useful for detecting low-abundance steroids, including Aldo and hybrid steroids and thus identifying steroid hormone-producing lesions.

Content of SI materials

Figure S1. Human adrenocortical steroidogenesis pathways. Four pairs of structural isomers exist in the pathway. 18-OH-Corticosterone (blue) is a structural isomer of cortisol (red) and cortisone (blue) is a structural isomer of aldosterone (red).

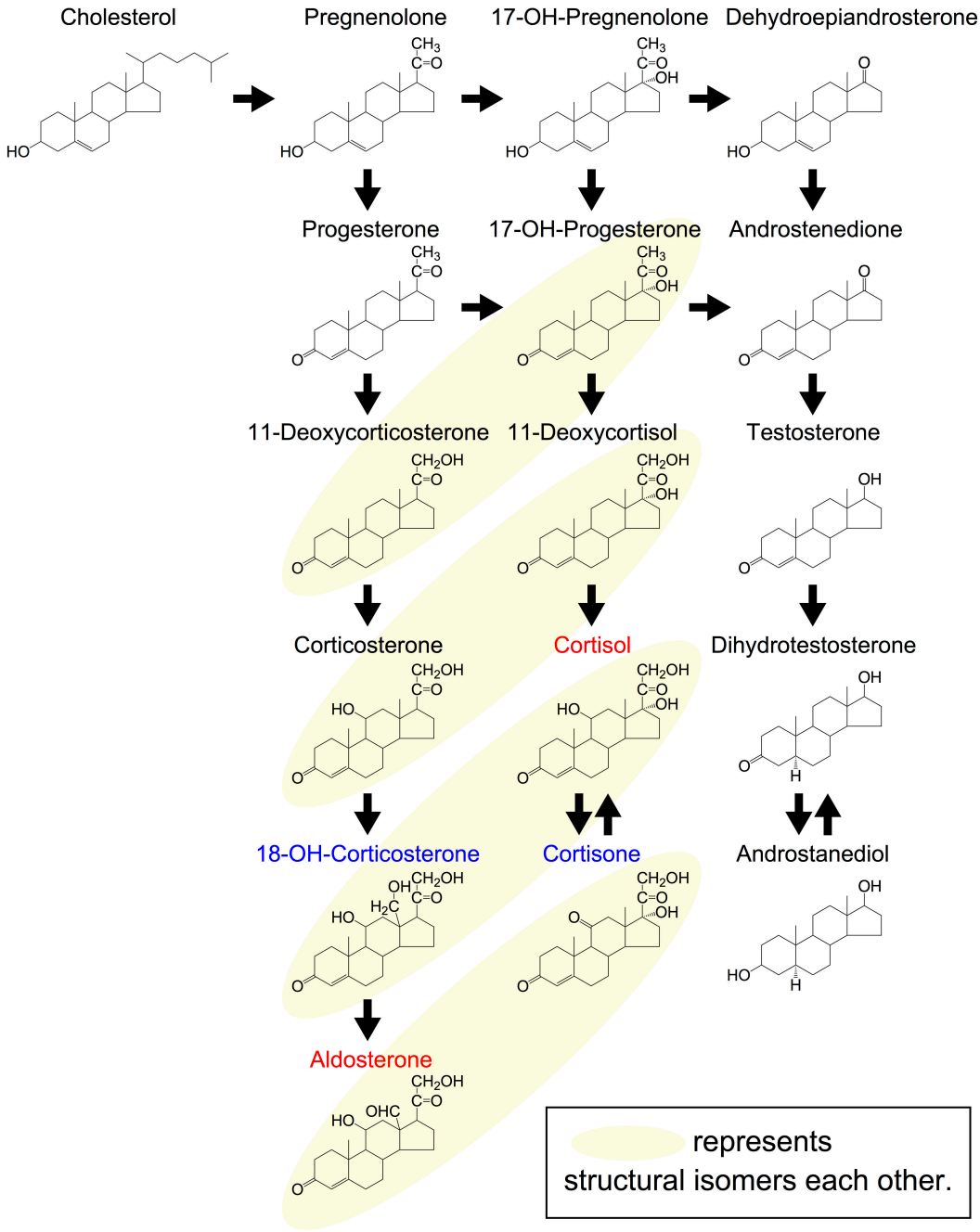

Figure S2. Comparison of matrix application methods for determination of MS^3 peak intensity of Aldo. The α-CHCA two-step method provided a clear view of GirT-Aldo distribution in the ZG.