Figure S1. Representative cases from in eight histologic subtypes of SCC (HE, ×10 magnification).

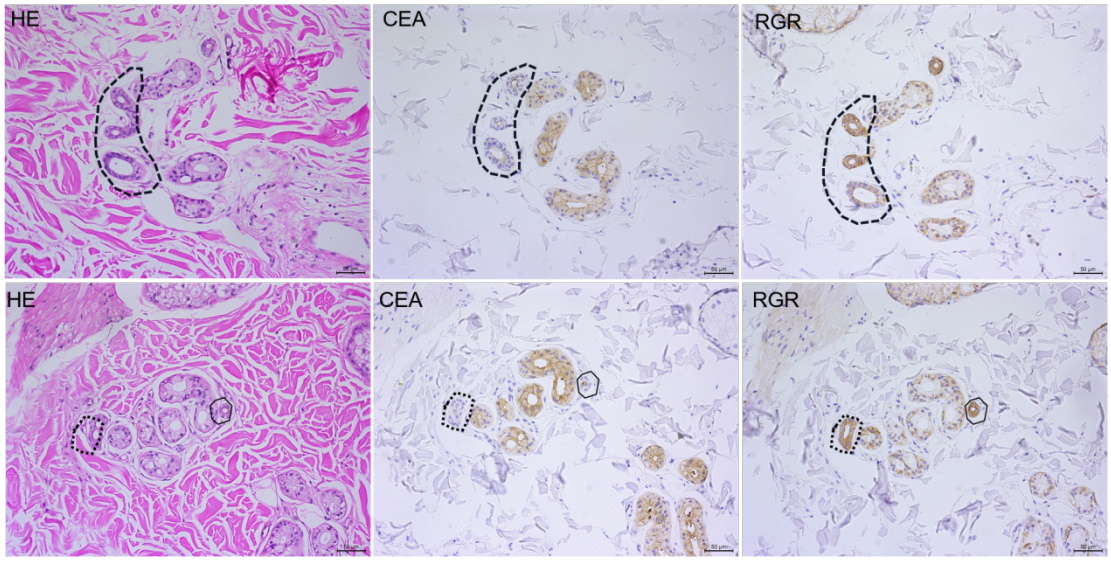

Figure S2. RGR expression in ductal epithelium cells (dotted line) was significantly stronger than that in glandular epithelium cells of eccrine glands labeled with CEA (HE, IHC, ×20 magnification).

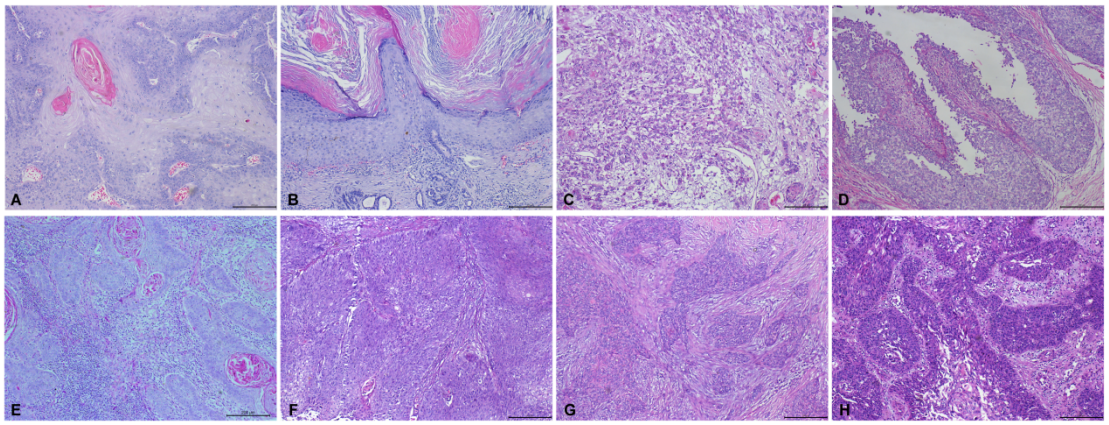

Figure S3. Compare RGR protein expression in eight histologic subtypes of SCC using Immunohistochemistry assay. A Common, B Keratoacanthoma-like, C Desmoplastic, D Spindle-Cell, E Verrucous, F acantholytic epithelioid, G Clear-Cell, H Adenosquamous. (×20 magnification)

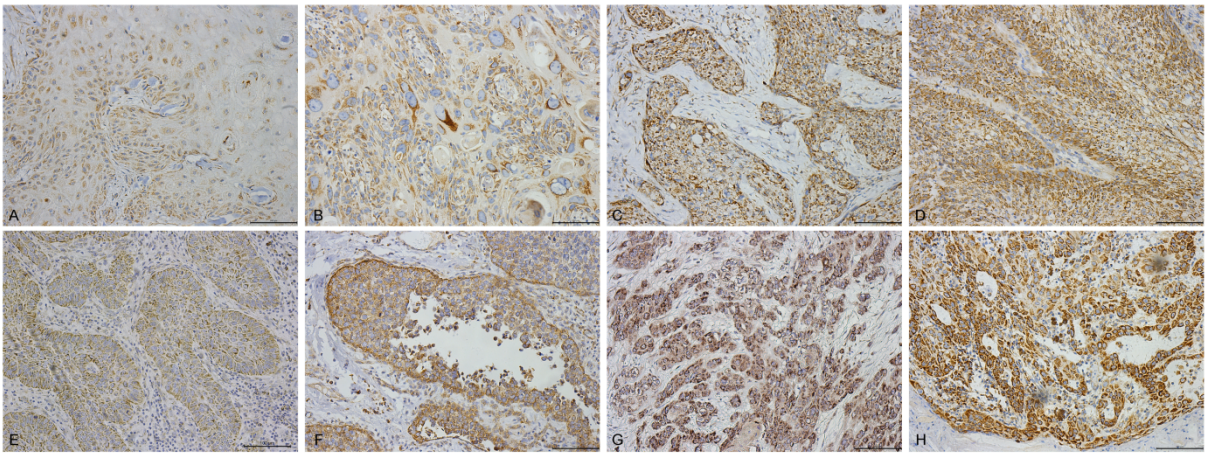

Figure S4. RGR RNA in situ hybridization (brown dots) of representative case from SCC by RNAscope analysis. A, poorly differentiated SCC. B, well differentiated SCC. a, b, the images of RGR RNA expression (brown dots) were analyzed by QuPath software (version 0.2.3). Cell nucleus: blue color. Scale bars indicate 20μm. C, Immunohistochemistry analysis of RGR expression between well differentiated regions of SCC and poorly differentiated areas from the same sample. C, Slide of SCC case was scanned by Leica software (ScanScope CS2) (Scale bars indicate 500μm). RGR expression in poorly differentiated areas of SCC (D-d1) (the blue dotted box, red asterisk) was significantly lower than in well differentiated regions (the green dotted box, orange dots) (D-d2). D, Scale bars indicate 200μm; d1-d2: Scale bars indicate 50μm.

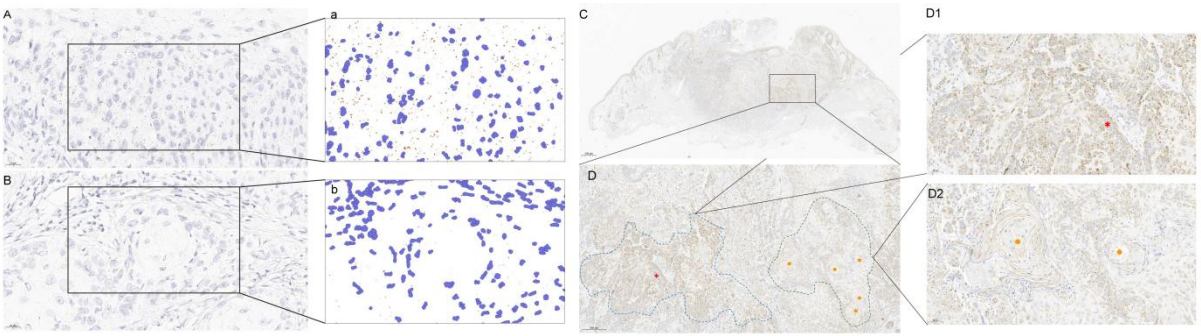

Figure S5. Immunofluorescence analysis of SCC co-stained for RGR (red) and involucrin (green) proteins. Selected co-staining image displayed that RGR expression in well differentiated regions (red asterisk) of SCC was significantly lower than in poorly differentiated areas (green polygon), whereas involucrin expression had the opposite trend.