Temperature-induced structural transitions in epidermal growth factor

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WHuman epidermal growth factor (EGF) consists of 53 amino acid (AA) residues, and it has a dynamic conformational structure. According to the known data, the amount of EGF AA residues in antiparallel β-sheets varies from 7 to 35%, while the amount of AA residues in α-helices varies from 0 to 23% depending on experimental conditions. Circular dichroism (CD) spectra for synthetic EGF with native AA sequence and EGF reduced by tris(2-carboxyethyl)phosphine were obtained on a Chirascan CD spectrometer at physiological pH during the heating from 20°C to 50°C. EGF has been dissolved in 0.01M phosphate buffer (pH 7.4). EGF concentration in obtained saturated solution was 495.3 μg/ml. Deconvolution of CD spectra was performed by BeStSel server. The amount of AA residues forming antiparallel β-sheets is significantly higher in reduced EGF than in native EGF (33% vs. 24%, P=0.012), while the content of α-helices is significantly lower (16% vs. 20%, P=0.033). Taken together, the EGF conformational state is almost identical at 20°C, 25°C, and 50°C, but at 35°C the highest amount of AA residues forming antiparallel β-sheets both in native and reduced EGF was observed (31% and 46%, respectively). In contrast, at 40°C the number of AA residues forming antiparallel β-sheets both in native and reduced EGF was the lowest (11% and 9%, respectively). The number of AA residues forming α-helices both in native and reduced EGF was minimal at 35°C (14% and 13%, respectively), and it was maximal at 40°C (24% for both). There is evidence that significant conformational changes occur in both native EGF and EGF with reduced disulfide bonds at the temperature between 35°C and 40°C. Based on known structural data, the EGF conformation observed at about 40°C is similar to PDB ID 1JL9: there are no β-strands, but just four residues making two beta bridges (Cys20 with Cys31 and Val34 with Tyr37). Exactly in such a relaxed state, EGF should be able to form a functional complex with its receptor.