

## Structural analysis of engineered cortisol binding sites on alpha-1 chymotrypsin

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### INTRODUCTION

Eczema is a term used to describe the skin condition that is inflamed or irritated. There are different types of eczema but, the most common one is atopic eczema. The other ones are contact, dyshidrotic, nummular, seborrheic, stasis. Each one has its own cause and reasons. Acute and chronic conditions can be observed. It can also be inherited like asthma and allergic rhinitis. It commonly occurs in children of age groups 5 years. About 20-30 percentage of children are affected. Not only in children it can also be observed in adults but, it sometimes shows up according to the conditions they are in and in some symptoms continue to show throughout their life. It isn't a contagious disease so it doesn't spread between people. There is a lot of research done in this field about how to treat eczema and various scientists gave their views. As the reason is still unknown, the treatment suggested is to use moisturizer to keep the skin hydrated all the time. It's good to include supplements good for skin like omega 3 fatty acids, citric acid in the diet.

6HGF is a protein which contains the engineered cortisol binding sites on alpha-1 chymotrypsin. This protein actually works on reducing the inflammation in the skin. This protein is short called as ACT. ACT contains the similar sequence as the CBG (corticosteroid binding globulin). By adding 15 amino acid sequences they converted ACT into surrogate CBG thereby creating new binding globulin (new BG). This new BG binds cortisol with 1.5 micromolar affinity and 33-fold lower affinity than the CBG, but shares a similar binding site. In this, the proteinase S to R transitions leading to a reduction of more than 200 fold in ligand affinity. This reduction is 10 folds more than the observed human CBG. This helps the protein to inhibit the cortisol much more better than the normal human CBG. Cortisol is a hormone well known to be released during stress conditions. But the production of cortisol doesn't directly influence the cause of eczema, but during stress conditions the production of cortisol can influence the cause of eczema. This can lead to eczema and skin flare. So mental health influences the cause of eczema. Structure title of 6HGF is Crystal Structure of Alpha 1-anti chymotrypsin variant New BG-II: a new binding globulin in complex with cortisol. Cited from journal J Struot Biol 201:169-189 published in the year 2019.

### EXPERIMENTALS

On searching for eczema in PDB the total structures appeared are 38. After applying filters it reduced to 3 structures. The selected structure is 6HGF. The resolution of this protein is 1.65 Å. R-value free is 0.187 and R-value work is 0.157. Two tests are done to know whether the protein structure is good and stable or not.

Test-1 : the R-value work should be roughly equal to 1/10 of resolution

Test-2 : the difference between R-value work and R-value free must be equal to or less than 0.05.

Macromolecules present in the protein are 2 molecules of Alpha-1 antichymotrypsin.

Small molecules present in the protein are HCY and EDO. The file is downloaded and viewed in PYMOL. The structure appeared in two colors i.e., green and cyan. They are compared by their sequence. Observe both the protein under secondary structure. Check for small molecules and observe hydrogen bonds in them.

The average hydrogen bond length of ligands is observed. It should be less than 3 Å.

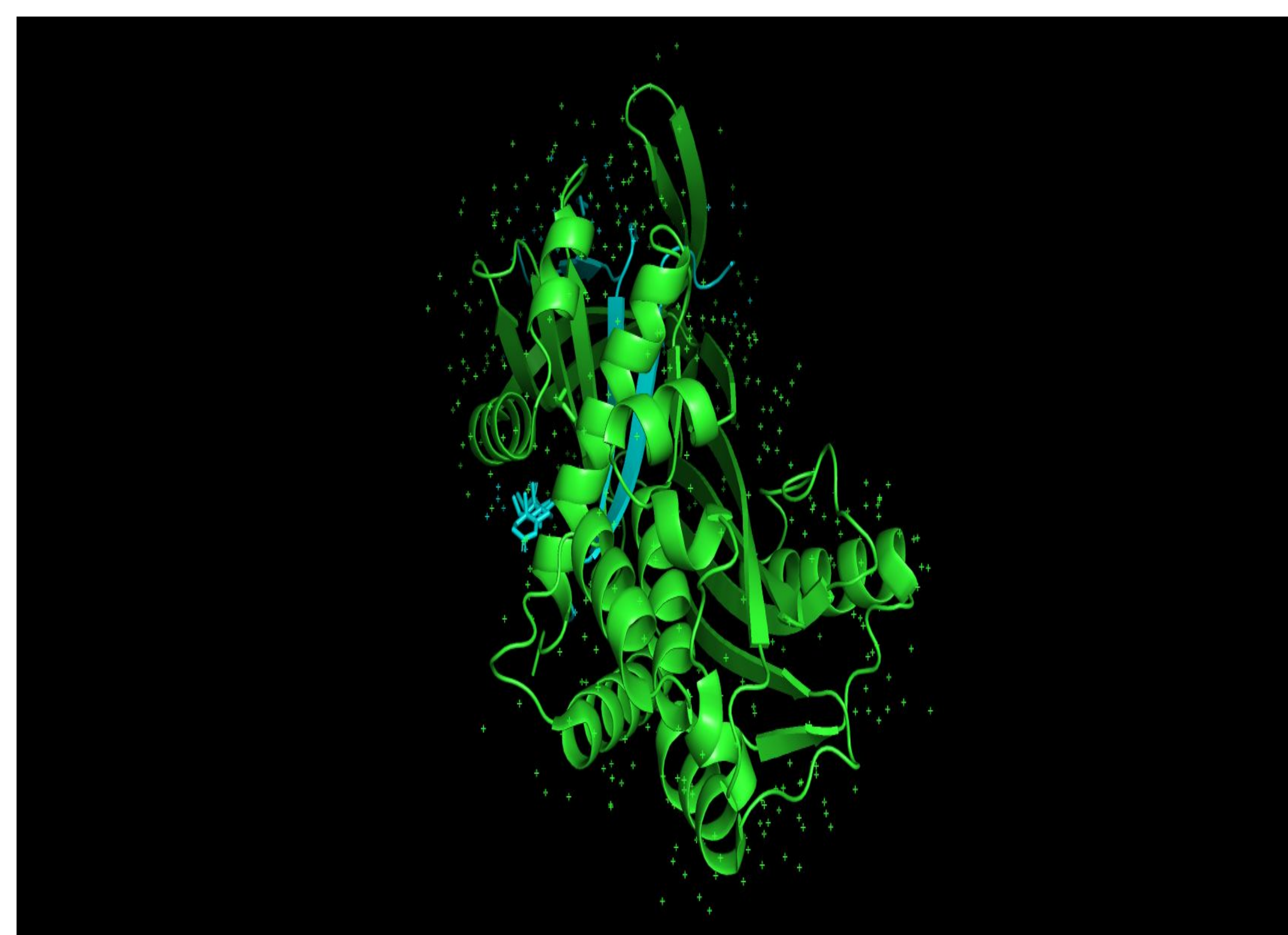


Figure 1. 3D Structure of ACT with cortisol binding sites viewed in PYMOL

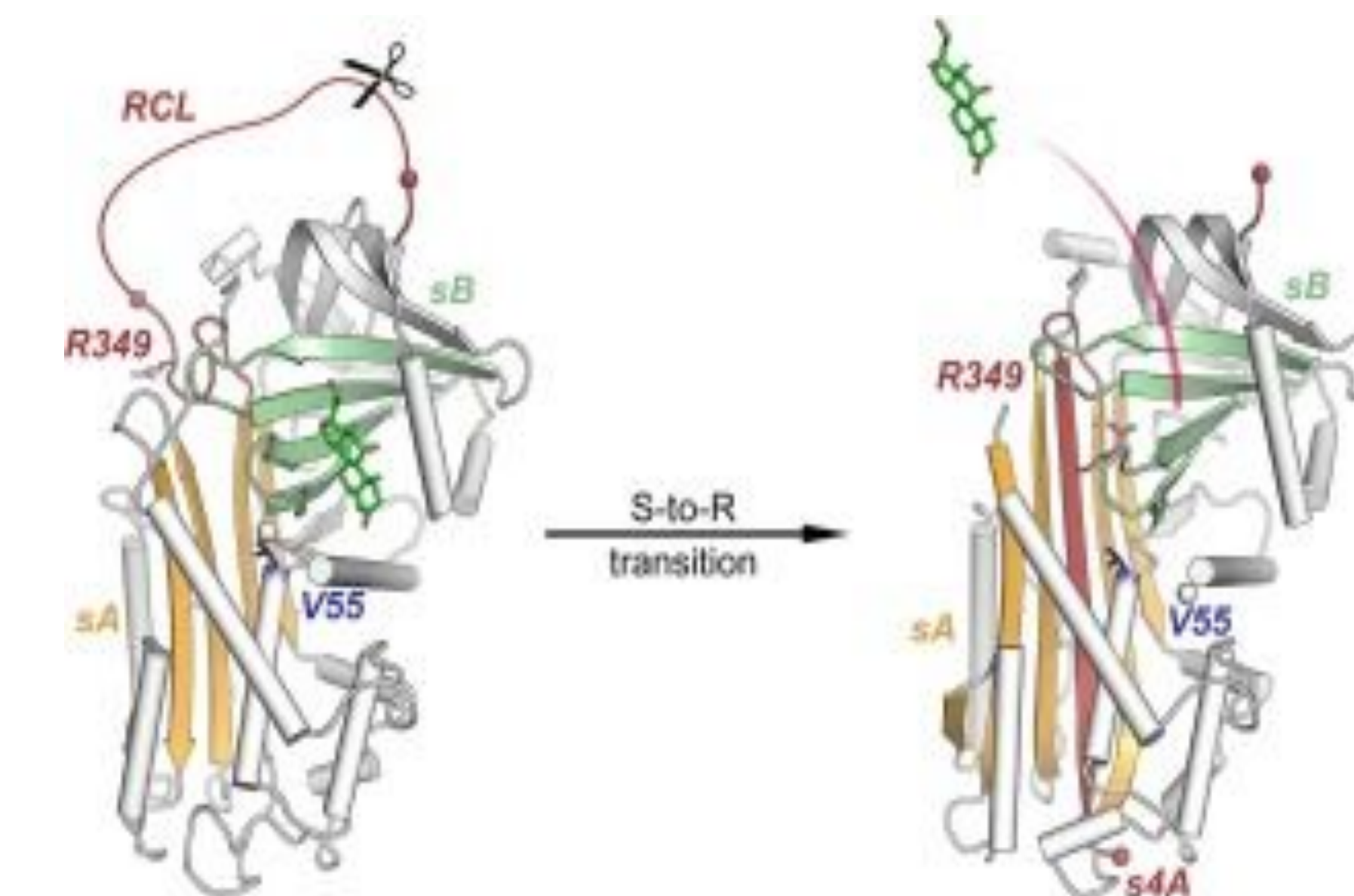


Figure 2 . ACT molecule showing S to R transition

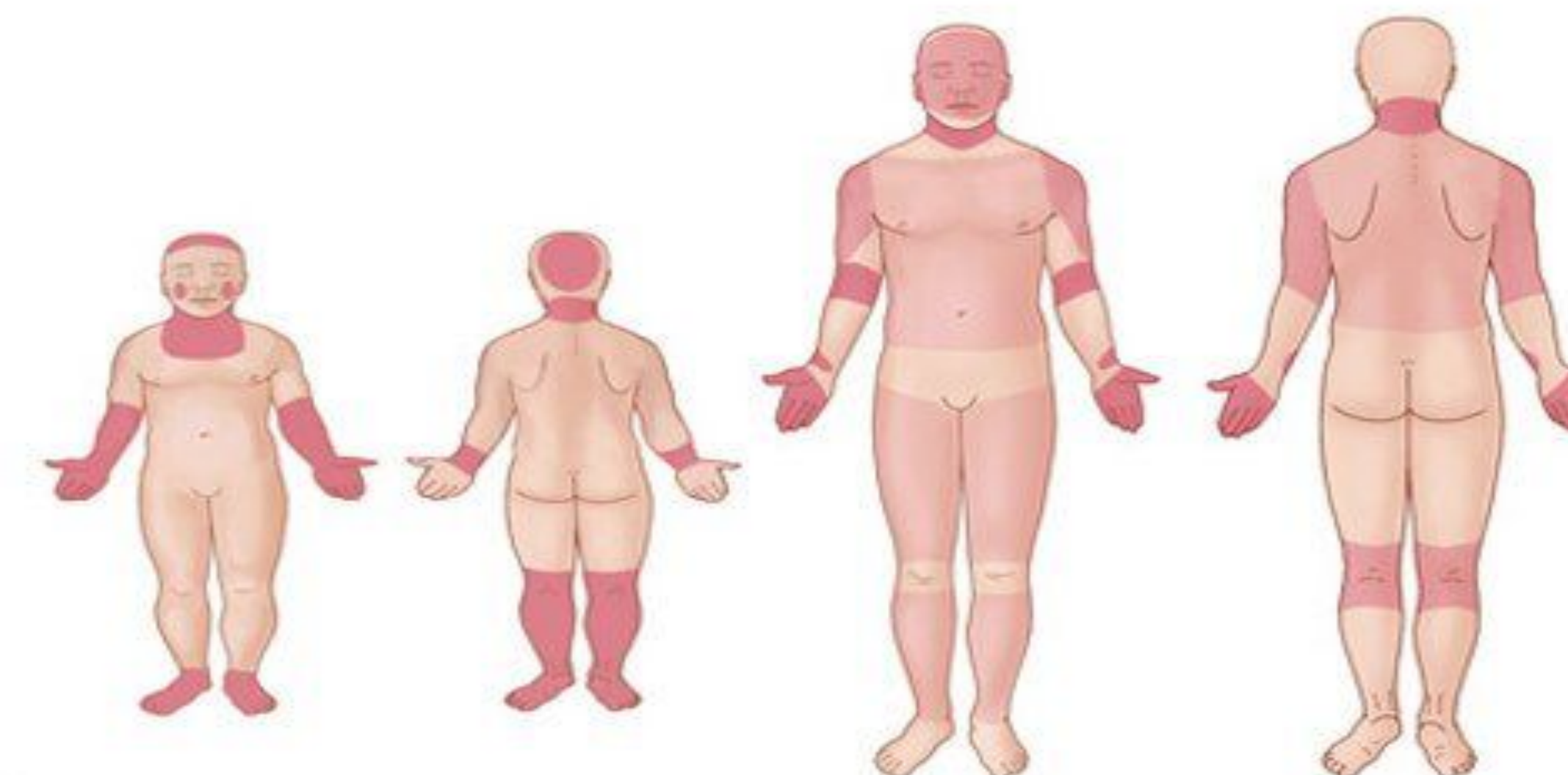


Figure 3 . Areas which are most affected by eczema

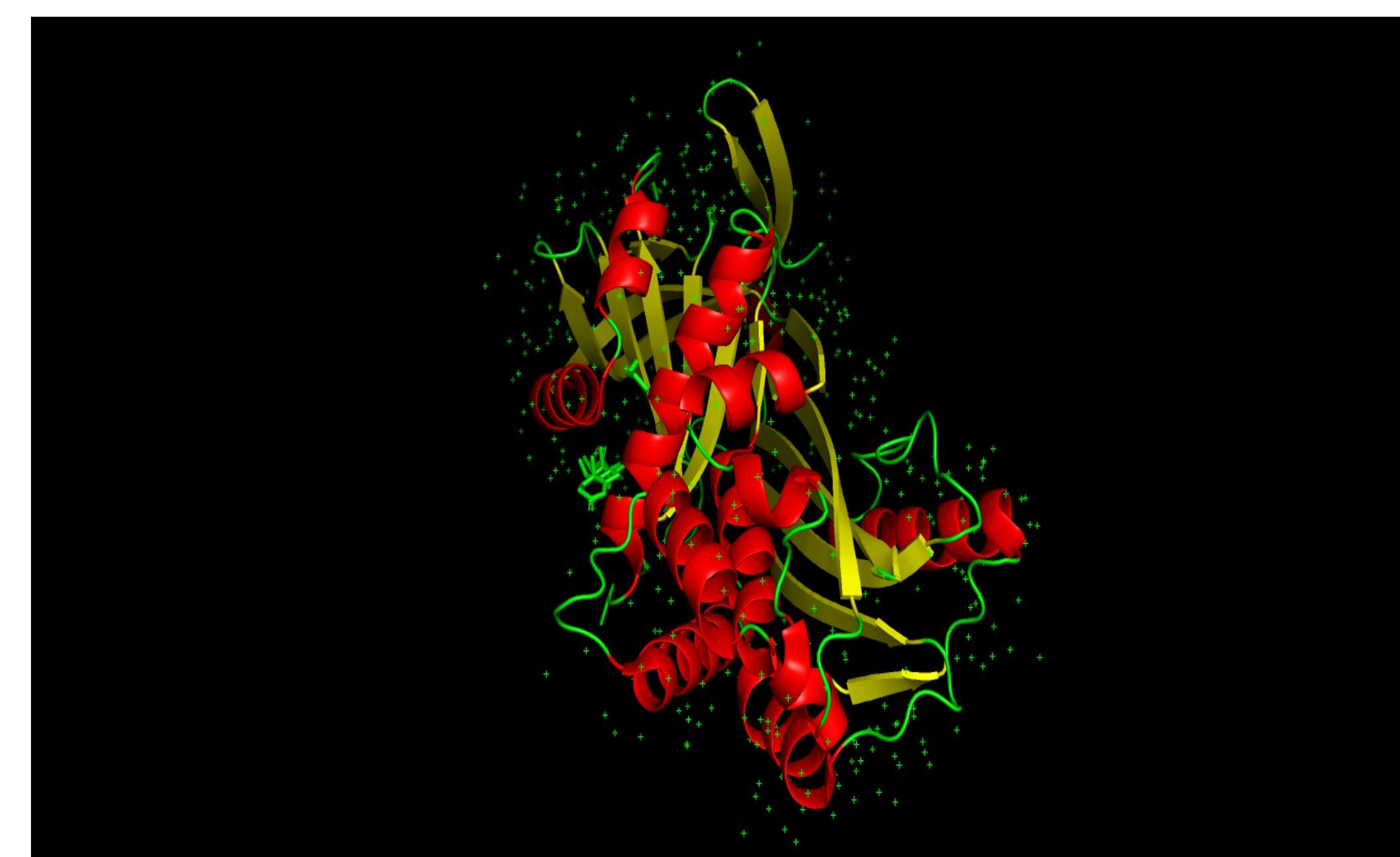


Figure 4. 6HGF molecule showing its secondary structure

### RESULTS & DISCUSSION

6HGF protein molecule is a stable protein as the difference between R-value work and R-value free is 0.03 which is less than 0.05.

As the compared sequence of green and cyan colored molecule is different it is said that the two molecules are different.

EDO of green molecule has 5 hydrogen bonds.

HCY of cyan molecule has 8 hydrogen bonds.

EDO of cyan molecule has 4 hydrogen bonds.

The average bond length of hydrogen bond is 2.88, so the structure is having strong hydrogen bonds.

This protein binds to the cortisol inhibiting it to cause the inflammation in the skin which may trigger it to cause eczema.

Practising meditation can decrease the chance of cause of eczema.

Good mental health can prevent the cause of eczema.

Bojungikgi-tang is the medicine used in Korea to treat eczema.

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