講　演　会

Protein surface decoration modulates cytosolic solubility and stability: exploring the effects of charge and hydrophobicity by *in-cell* NMR

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Biological life relies on delicately tuned functional protein networks that have to work in complex, highly crowded environments. In most cases the proteins need to fold into a well-defined three-dimensional structure, where the stability is tuned for optimal turnover and function. Furthermore, for such networks to be plastic and reactive the non-specific protein interactions have to be weak and short-lived, so called transient interactions: the transient interactions are frequent and long enough for encounter complexes to form to enable a specific partner to be found, but short enough to prevent proteins to get stuck in non-productive interactions.

Here we show that surface properties of proteins affect the intra-cellular solubility as well as the stability, and the importance of the surface is further underlined from the rapid evolution seen on protein surfaces, resulting in that structural and functional homologues from different environments can show very different surface properties. We use electroporation to transfer isotope labeled proteins into mammalian cells and directly measure the stability change by in-cell NMR. Different proteins show different stability response on the in-cell environment, i.e. the sequential details and transient interactions, by the protein surface, modulate protein stability and thereby function. However, the precise mechanism how the surface properties affect the transient interactions are yet to be elucidated.

To further address this question we use in-cell NMR to quantify how electrostatic and hydrophobic interactions influence solubility of globular proteins by observation of protein rotational correlation times. We modulated the surface properties by a large number of point mutations and determined how these changes affects the protein solubility in living cells. We find that an overall negative charge is necessary, and that the rotational freedom can be described as a plane in a charge-hydrophobicity space. The two determinants in play help to compensate for functional entities that may reduce solubility: a low net charge can be compensated by decreased hydrophobicity and vice versa.

To test the generality in our findings we also studied a slightly larger human protein with a different fold and we find that also this fall on the very same plane. In addition to these global properties the in-cell solubility is modulated by charge distribution and surface topology.

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