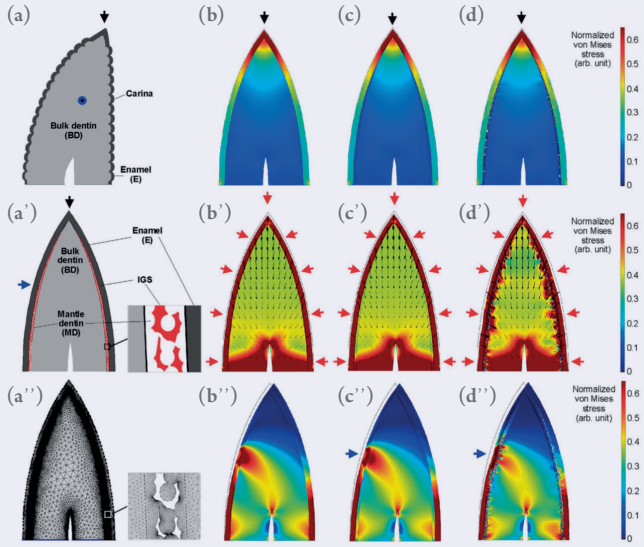

Fig. 4: Two-dimensional multi-tissue mechanical simulations of a long and sharp saurischian tooth. (a) Lingual view. (a') Mesial or distal view. (a'') Mesh structure of the tooth model generated by the finite-element analysis software. Black, blue and red arrows show the directions of the applied external forces. (b-d) A force acts on the apex of a saurischian tooth, which consists of various dental compositions near the dentine-enamel junction (DEJ). (b'-d') A net force acts normally on the whole enamel surface of a saurischian tooth, which includes various dental compositions near the DEJ. (b''-d'') A force acts on the lingual or labial surface of a saurischian tooth, which consists of various dental compositions near the DEJ. Abbreviations: E, enamel; BD, bulk dentine; MD, mantle dentine. [Reproduced from Ref. 2]

From the evolutionary point of view, the MD-IGS structures might be much more suitable for long and sharp saurischian hunting teeth because these structures function like a damper, which means that they could protect the teeth from breakage while the latter are tearing at large preys. (Reported by Kai-Dee Lee and Chun-Hsiang Huang)

This report features the works of Yao-Chang Lee, Robert R. Reisz, and their co-workers published in Sci. Rep. ***5****, 12338 (2015), and of Chun-Chieh Wang, Robert R. Reisz, and their co-workers published in Sci. Rep.* ***5****, 15202 (2015).*

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How Do Pathogenic Bacteria Disable the Host Immune System in Phagocytosis?

Phagocytosis, performed by an organism's immune system, is a crucial mechanism to remove pathogens and cell debris. This mechanism is triggered by actin polymerization, which is orchestrated by various actin-regulating proteins such as CapG, gelsolin, diaphanous, WASP, WIP and VASP. Disrupting the expression or function of these proteins impairs phagocytosis in macrophages, as supported by previous studies. In the fourteenth century, a highly contagious pathogen, *Y. pestis*, caused the outbreak and spread of the bubonic plague, resulting in about 30–60 % death of the European population.

For a pathogen to survive in a host organism, halting the process of actin assembly is a common and useful strategy. In this regard, the pathogenic *Yersinia* species attacks a host immune system through the type-III secretion systems to inject bacterial effector proteins across the bacterial and host cell membranes and to subvert the phagocytic cells. YopO, one such effector, can interfere with actin cytoskeleton to inactivate phagocytosis.

To unmask the important molecular mechanisms behind this phenomenon, Robert C. Robinson and his co-workers solved the structure of the complex of *Y. enterocolitica* YopO with actin using BL13B1.[1] The crystal structure of YopO-actin showed that the actin molecule is sandwiched between the GDI and kinase domains of YopO (Fig. 1(a)). The Rac1 and actin binding sites on the GDI domain and the active site on the kinase domain are found in three separate areas, indicating that these interactions might occur

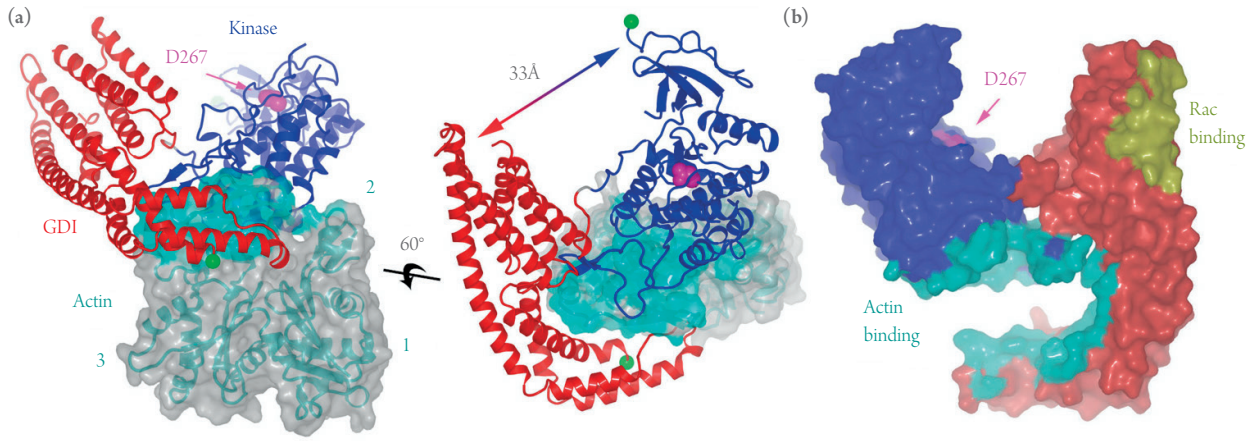

Fig. 1: Overall structure of the YopO-actin complex. (a) Two views of the structure (front and top). YopO consists of a GDI domain (shown in red) and a kinase domain (blue). Catalytic residue D267 is displayed as magenta spheres. (b) Surface representation. Based on the topology, the two binding sites and one active site are clearly located in separate places on YopO. [Reproduced from Ref. 1]

simultaneously (Fig. 1(b)). In addition, activation of the kinase is induced upon actin binding, which provides stabilizing interactions with the catalytic loop.

Regarding the sequestration of actin monomers, Fig. 2(a) indicates that the formation of the actin filament[2] is disrupted through steric hindrance upon YopO binding. In addition, biochemical analyses by spectrofluorimetry and autophosphorylation both indicated that 2-μm YopO WT and nRac (with mutation at the Rac-interaction interface of YopO) can almost eliminate actin polymerization and perform autophosphorylation (Figs. 2(b) and 2(c)). Subsequently, all mutants have a similar period for elution in a gel-filtration chromatograph. The structural folds of these mutants are thus expected to be correct (Fig. 2(d)).

According to a previous report by the authors, many actin-binding proteins bind to subdomain 1 or 3 of actin.[3] As shown in Figs. 3(a)-3(c), four actin-regulating proteins, including profilin, the G-actin-binding domain of VASP, the gelsolin domain 1-3[4] and the WH2 motif, might form ternary complexes with YopO and actin without steric conflict. According to Fig. 1(b), the catalytic cavity of the kinase domain is nearer actin. The authors thus speculated that YopO-bound actin might serve as a bait to recruit kinase substrates for phosphorylation. This phosphorylation assay *in vitro* supports the hypothesis in that all actin-binding proteins were phosphorylated except CapG and Twf1 (Fig. 3(d)). Taken together, the data indicated that the YopO-bound actin prevents polymerization because of the severe steric clash, while the actin-regulating proteins are recruited and phosphorylated by YopO.

In summary, the authors proposed a model to impede the actin dynamics with three parallel paths to disable phagocytosis by (i) suppressing signal transduction using sequestration of Rac and Rho, both contributing to mediate the actin assembly for a phagocytic cup, (ii) blocking polymerization at the host-pathogen contact interface via sequestration of actin, and (iii) down-regulating polymerization through phosphorylation of actin-binding proteins (Fig. 4). In a nutshell, *Y. enterocolitica* has developed its own way with YopO to survive the host immune system. (Reported by Chun-Hsiang Huang)

This report features the work of Robert C. Robinson and his colleagues published in Nature Struct. Mol. Biol. **22**, *248 (2015).*

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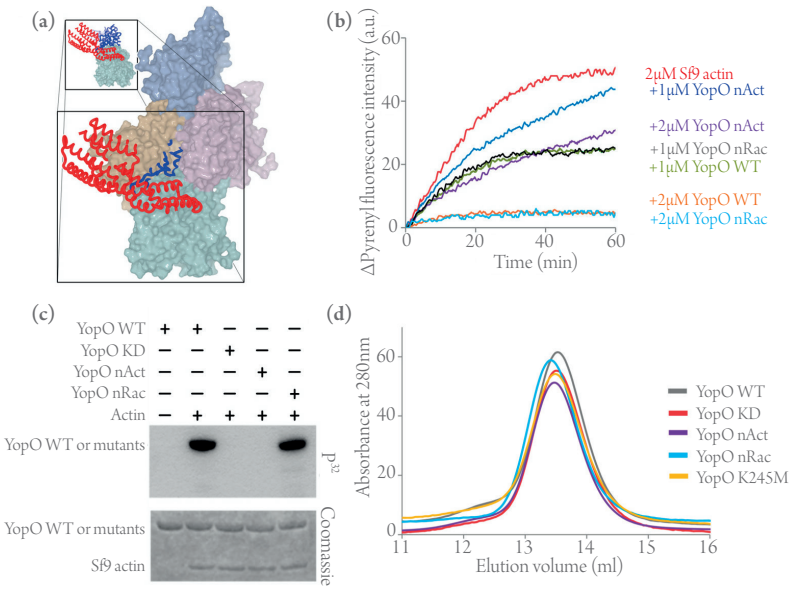

Fig. 2: Mechanism of actin-monomer sequestration. (a) Incompetent actin polymerization indicated by superimposition of the YopO-actin complex on the actin filament. (b) Pyrene-actin polymerization assay. (c) Autophosphorylation assay. (d) Size-exclusion chromatograms of WT YopO and mutants. [Reproduced from Ref. 1]

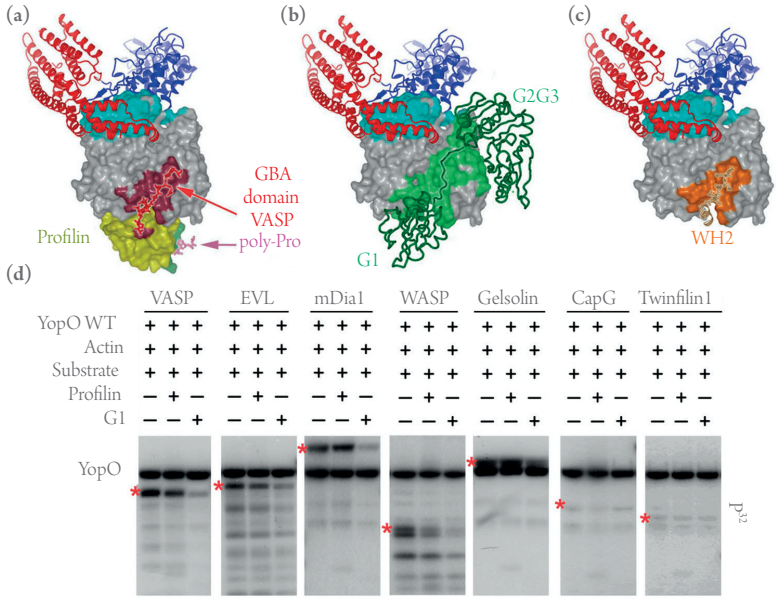

Fig. 3: Interaction and phosphorylation of actin-binding proteins. (a) The binding sites of profilin and GAB domain of VASP are shown in yellow and red, respectively. (b) The binding site of gelsolin domain 1–3 is shown in green. (c) The binding site of WH2 is shown in ocher. (d) Phosphorylation of actin-binding proteins by YopO. Red asterisks indicate the molecular weights of the substrates. [Reproduced from Ref. 1]

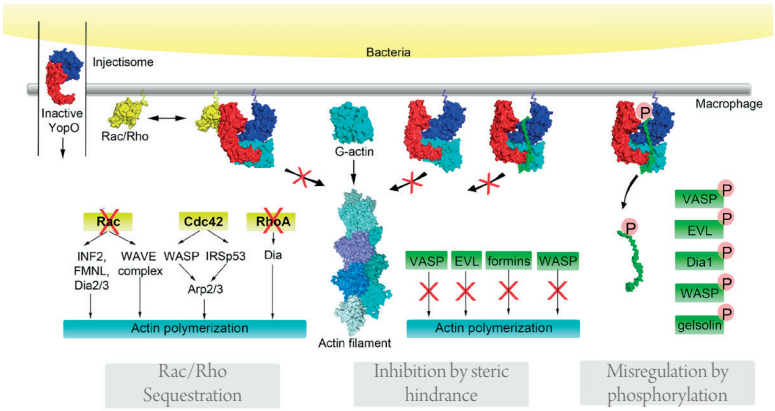

Fig. 4: Model for disabling actin polymerization by YopO. P, phosphorylation; Rac/Rho, Rac and/or Rho. [Reproduced from Ref. 1]