experience spontaneous inflammasome activation and paracrine IL-1 signalling, which is sufficient to cause symptoms, such as skin inflammation and epidermal hyperplasia.

[005] Although the function of NLR proteins in systemic inflammation is well established, less is known about their roles in organ-specific immune response and tissue homeostasis, particularly in epithelial tissues such as, for example, the skin. Apart from forming a structural barrier, human skin actively interacts with the immune system in guarding against invading pathogens and tissue damage. On the other hand, chronic unresolved skin inflammation can result in a variety of dermatological diseases and promote the development of both benign and malignant epithelial skin lesions.

[006] Thus, there is a need for methods and agents for treating or preventing skin disorders and determining cancer susceptibility.

## SUMMARY

[006a] In one aspect, the present disclosure refers to a method of determining the likelihood or predisposition of a subject in developing MSPC (multiple self-healing palmoplantar carcinoma) or FKLC (familial keratosis lichenoides chronica), comprising detecting one or more mutations in the NLR family, pyrin domain containing protein 1 (NLRP1) in a sample obtained from the subject, wherein when one or more NLRP1 mutations are located at its Pyrin (PYD) and/or LRR (leucine-rich repeats) domain, the subject has increased likelihood or predisposition in developing MSPC (multiple self-healing palmoplantar carcinoma) or FKLC (familial keratosis lichenoides chronica). In another aspect, the present disclosure refers to a method of determining whether a skin inflammation in a subject is caused by MSPC (multiple self-healing palmoplantar carcinoma) or FKLC (familial keratosis lichenoides chronica), comprising detecting one or more mutations in the NLR family, pyrin domain containing protein 1 (NLRP1) in a sample obtained from the subject, wherein when one or more NLRP1 mutations are located at its PYD (Pyrin) and/or LRR (leucine-rich repeats) domain, the skin inflammation in the subject is caused by MSPC (multiple self-healing palmoplantar carcinoma) or FKLC (familial keratosis lichenoides chronica). In another aspect, the present disclosure refers to a method of determining the likelihood or predisposition of a subject in developing MSPC (multiple self-healing palmoplantar carcinoma), FKLC (familial keratosis lichenoides chronica), or MSPC-squamous cell carcinomas (MSPC-SCC), comprising detecting one or more mutations in the NLR family, pyrin domain containing protein 1 (NLRP1) in a sample obtained from the subject, wherein when one or more NLRP1 mutations result in one or more amino acid substitutions selected from the group consisting of A54T, M77T, and A66V, or when one or more NLRP1 mutations result in the deletion of the amino acid sequence starting from phenylalanine at position 787 to arginine at position 843 (F787 to R843 or F787_R843del) , the subject has increased likelihood or predisposition in

developing MSPC, FKLC, or MSPC-SCC. In another aspect, the present disclosure refers a method of determining whether a skin inflammation in a subject is caused by MSPC (multiple self-healing palmoplantar carcinoma) or FKLC (familial keratosis lichenoides chronica), comprising detecting one or more mutations in the NLR family, pyrin domain containing protein 1 (NLRP1) in a sample obtained from the subject, wherein when one or more NLRP1 mutations result in one or more amino acid substitutions selected from the group consisting of A54T, M77T, and A66V, or when one or more NLRP1 mutations result in the deletion of the amino acid sequence starting from phenylalanine at position 787 to arginine at position 843 (F787 to R843 or F787_R843del), the skin inflammation in the subject is caused by MSPC or FKLC.

[007] In one example, the present disclosure refers to a method of treating or preventing an autoimmune skin disorder and/or inflammatory skin disorder in a subject in need thereof, comprising administering a therapeutically effective amount of an inhibitor capable of inhibiting the activation of inflammasome sensor NLRP1 (Nucleotide-binding domain, leucine-rich repeat containing (NLR) family, pyrin domain containing protein 1 – NLPR1).

[008] In another example, the present disclosure refers to a method of treating or preventing an autoimmune skin disorder and/or inflammatory skin disorder in a subject in need thereof, comprising administering a therapeutically effective amount of an agent that prevents the secretion of stress responsive secreted factors, known pro-inflammatory cytokines, keratinocytes differentiation markers, inflammasome-dependent cytokines, and growth factors in the skin.

[009] In yet another example, the present disclosure refers to a method of treating or preventing an autoimmune skin disorder and/or an inflammatory skin disorder in a subject in need thereof, comprising administering a therapeutically effective amount of an agent that reduces the effect of inflammasome-dependent cytokines.

[0010] In a further example, the present disclosure refers to a method of determining whether a skin inflammation in a subject is an inflammatory skin disorder and/or an autoimmune skin disorder, comprising detecting NLRP1 mutation in a sample obtained from the subject.

[0011] In another example, the present disclosure refers to a method of determining the likelihood (or predisposition) of a subject in developing an inflammatory skin disorder and/or an autoimmune skin disorder, comprising detecting NLRP1 mutation in a sample obtained from the subject.

## CLAIMS

1. A method of determining the likelihood or predisposition of a subject in developing MSPC (multiple self-healing palmoplantar carcinoma) or FKLC (familial keratosis lichenoides chronica), comprising detecting one or more mutations in the NLR family, pyrin domain containing protein 1 (NLRP1) in a sample obtained from the subject, wherein when one or more NLRP1 mutations are located at its Pyrin (PYD) and/or LRR (leucine-rich repeats) domain, the subject has increased likelihood or predisposition in developing MSPC (multiple self-healing palmoplantar carcinoma) or FKLC (familial keratosis lichenoides chronica).

2. A method of determining whether a skin inflammation in a subject is caused by MSPC (multiple self-healing palmoplantar carcinoma) or FKLC (familial keratosis lichenoides chronica), comprising detecting one or more mutations in the NLR family, pyrin domain containing protein 1 (NLRP1) in a sample obtained from the subject, wherein when one or more NLRP1 mutations are located at its PYD (Pyrin) and/or LRR (leucine-rich repeats) domain, the skin inflammation in the subject is caused by MSPC (multiple self-healing palmoplantar carcinoma) or FKLC (familial keratosis lichenoides chronica).

3. A method of determining the likelihood or predisposition of a subject in developing MSPC (multiple self-healing palmoplantar carcinoma), FKLC (familial keratosis lichenoides chronica), or MSPC-squamous cell carcinomas (MSPC-SCC), comprising detecting one or more mutations in the NLR family, pyrin domain containing protein 1 (NLRP1) in a sample obtained from the subject, wherein when one or more NLRP1 mutations result in one or more amino acid substitutions selected from the group consisting of A54T, M77T, and A66V, or when one or more NLRP1 mutations result in the deletion of the amino acid sequence starting from phenylalanine at position 787 to arginine at position 843 (F787 to R843 or F787_R843del), the subject has increased likelihood or predisposition in developing MSPC, FKLC, or MSPC-SCC.

4. A method of determining whether a skin inflammation in a subject is caused by MSPC (multiple self-healing palmoplantar carcinoma) or FKLC (familial keratosis lichenoides chronica), comprising detecting one or more mutations in the NLR family, pyrin domain

containing protein 1 (NLRP1) in a sample obtained from the subject, wherein when one or more NLRP1 mutations result in one or more amino acid substitutions selected from the group consisting of A54T, M77T, and A66V, or when one or more NLRP1 mutations result in the deletion of the amino acid sequence starting from phenylalanine at position 787 to arginine at position 843 (F787 to R843 or F787_R843del), the skin inflammation in the subject is caused by MSPC or FKLC.

5. The method of any one of claims 1 to 4, wherein the sample is selected from the group consisting of bodily fluid, and skin.

6. The method of claim 5, wherein the skin is selected from the group consisting of epidermis, glabrous skin, plantar skin, and epidermal appendages.

7. The method of claim 5, wherein the skin is keratinocytes and/or fibroblast.