

## Autoantibodies in idiopathic inflammatory myopathies

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- Diagnostic marker with pathogenetic significance
  - Diagnostic marker for indicated disease
  - Colored circles indicate markers for primary screening
  - Indicative autoantibody
  - Occasionally associated autoantibodies with marker function for other diseases
  - Autoantibodies, which may be found randomly associated but without disease specificity and without any diagnostic significance for the disease mentioned.
- ▶ Cited **literature** is marked with **red** numbers and linked with the authors given at the end of the document. By clicking the hand symbol (  ) one returns to the top of the table.
- ▶ **Autoantibodies** cited in the following tables are linked with their respective descriptions.
- ▶ The indicated values of **sensitivity** and **specificity** crucially depend on the respective test methods, on genetic and ethno-geographical variables and on the selection of tested patient and control populations, which is reflected by the considerable variations of the indicated data. Therefore the given figures may be regarded as an approximate guide for the selection of adequate tests for a given clinical situation. For this reason also qualitative estimates such as “low”, “medium” or “high” were used.



## Autoantibodies in idiopathic inflammatory myopathies

### Dermatomyositis (DM)

| Autoantibodies                               | Sens [%]    | Spec [%] | Disease associations          |
|--|-------------|----------|-------------------------------|
| ● ANA- IIFT                                  | 50 - 80     | low      | multiple                      |
| <b>Myositis specific antibodies (MSA) *7</b> |             |          |                               |
| ● TIF1-γ *1                                  | 14 - 31     | high *2  | JDM, ADM, CaM 58              |
| ● MDA5 (CADM-140)                            | 11 - 35 *4  | high *2  | CADM, ILD, MCL 17, 45, 28, 32 |
| ● NXP2 (MJ)                                  | up to 30 *5 | high *2  | JDM, ADM, (CaM?) 28           |
| ● SAE  | up to 8 *6  | high *2  | ADM 64                        |
| ● Mi-2                                       | 5 - 30      | > 95     | DM (PM, IBM) 6, 33, 62, 64    |
| ● Alanyl-tRNA synthetase (PL12)              | up to 6     | high *3  | PM, DM, ILD 6, 25             |
| ● Asparaginyl-tRNA synthetase (KS)           | < 1         | high *3  | PM, DM, ILD 6                 |
| ● Glycyl-tRNA synthetase (EJ)                | < 1         | high *3  | PM, DM, ILD 23a               |
| ● Histidyl-tRNA synthetase (Jo-1)            | 9 - 20      | > 95 *3  | PM, DM, ILD, OM 6, 33, 25, 64 |
| ● Isoleucyl-tRNA synthetase (OJ)             | < 1         | high *3  | PM, DM, ILD 6                 |
| ● Phenylalanyl-tRNA synthetase (ZO)          | unknown     | unknown  | PM, DM, ILD                   |
| ● Threonyl-tRNA synthetase (PL7)             | < 3         | high *3  | PM, DM, ILD 6, 25             |
| ● Tyrosyl-tRNA synthetase (Ha, YRS)          | unknown     | unknown  | PM, DM, ILD                   |
| ● SRP  | 0 - 3       | high *3  | PM, DM, NAM 6, 33, 64         |

\*1 The antibodies anti-TIF1-γ (150 kDa), -β (100 kDa), -α (140 kDa) exist in various combinations. By means of immunoprecipitation about 98,8 % of anti-TIF1 antibodies can be demonstrated with exception of solitary anti-TIF1-β (20). Anti-TIF1-γ has been demonstrated in 23 - 29 % of patients with juvenile dermatomyositis (22, 57), and in 13 - 30 % in the cases of adult dermatomyositis (22, 19, 57, 56). Carcinomas were present in about 50 - 75 % of the anti-TIF1 positive patients (20, 19).

\*2 The antibodies are regarded as specific for DM.

\*3 The figures of specificity refer to the idiopathic inflammatory myopathies on the whole (DM, PM, DM/PM-overlap).

\*4 The figures given for prevalence refer particularly on studies in Asian patient populations. An American study revealing a prevalence of 13 % noted also pronounced cutaneous and mucocutaneous lesions ("dermatopulmonary syndrome") (17).

\*5 Anti-NXP2 are found in 19 - 29 % of patients with juvenile dermatomyositis, associated with pronounced muscle weakness, calcinosis, joint contractures, and muscle cell necrosis (14, 23, 28). Antibody prevalence in early adult dermatomyositis in USA and Europe was 17 - 30 % (17, 9) and 1,6 % in Japan (28). In the adult form there were also found some associations with carcinomas and 8 % of the afflicted patients suffered from PM (9).

\*6 Lower prevalence (< 2 %) in Japanese studies.

\*7 According to Troyanov (59) the MSA and MAA, except anti-Mi-2, anti-SS-A/Ro, and anti-SS-B/La, have been classified as „overlap-antibodies“ in the following three groups:

1. anti-synthetases: anti-Jo1, -OJ, -EJ, -KS, -PL7, -PL12.

2. antibodies associated with SSc: anti-centromeres, -Scl 70, -Th/To, -RNA-polymerases, -PM/Scl, -U1snRNP, -U2-snRNP, -U3-snRNP, -U5snRNP, -Ku.

3. other overlap-antibodies: anti-SRP, -nucleoporin.

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## Autoantibodies in idiopathic inflammatory myopathies

Continuation

| Dermatomyositis                                |            |          |  |
|--|------------|----------|--|
| Autoantibodies                                 | Sens [%]   | Spec [%] | Disease associations   |
| <b>Myositis specific antibodies (MSA) *7</b>   |            |          |  |
| ● PMS1   | 8          | unknown  | DM, PM, aplA <span style="float:right">8</span>              |
| ● PMS2   | 4          | unknown  | DM, PM <span style="float:right">8</span>                    |
| ● MLH1   | 4          | unknown  | DM, PM <span style="float:right">8</span>                    |
| ● DNA-PK <sub>CS</sub>                         | 2          | unknown  | DM, PM <span style="float:right">8</span>                    |
| ● Mas  | 1          | unknown  | DM, PM, AIH <span style="float:right">6</span>               |
| <b>Myositis associated antibodies (MAA) *7</b> |            |          |  |
| ● PM/Scl                                       | up to 13   | medium   | DM, PM, OM <span style="float:right">61, 48, 5, 6, 33</span> |
| ● Ku   | 1          | unknown  | DM, PM, OM <span style="float:right">6, 64</span>            |
| ● Fibrillarin                                  | 4          | low      | DM, PM, OM <span style="float:right">33</span>               |
| ● U1-snRNP (U1-70K)                            | 4          | low      | MCTD, SLE, SS <span style="float:right">6, 33, 10, 64</span> |
| ● SS-A/Ro 60                                   | 4          | low      | SLE, SS <span style="float:right">6, 64</span>               |
| ● SS-A/Ro 52                                   | 22 - 24    | low      | SS, SLE <span style="float:right">6, 33</span>               |
| ● SS-B/La                                      | 3 - 13     | low      | SS, SLE <span style="float:right">6, 33</span>               |
| <b>Other antibodies</b>                        |            |          |  |
| ● Histone (H1)                                 | 17         | low      | SLE <span style="float:right">34</span>                      |
| ● Argonaute 2 (Su)                             | 4 - 9      | low      | PM, DM, SLE, MCDT, SS <span style="float:right">53</span>    |
| ● Endothelial cell                             | 36         | low      | multiple <span style="float:right">12</span>                 |
| ● Proteasome (20S; αC9)                        | 62         | low      | DM, SLE <span style="float:right">15</span>                  |
| ● ADAM 10                                      | casuistics | low      | DM, ILD <span style="float:right">21</span>                  |
| ● 50 kDa-Muscle membrane protein               | 15 - 20 *8 | low      | DM, PM, SSC, SLE, RA <span style="float:right">54</span>     |
| ● Myo22/25                                     | 8          | low      | DM, PM <span style="float:right">35</span>                   |
| ● 56 kDa-Kern-Protein                          | 85 - 90    | low      | JDM, ADM, PM <span style="float:right">2, 7, 13</span>       |
| *8 Elisa with rhabdomyosarcoma cells (TE671)   |            |          |  |

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## Autoantibodies in idiopathic inflammatory myopathies

| Polymyositis   |            |                 |                             |
|--|------------|-----------------|-----------------------------|
| Autoantibodies   | Sens [%]   | Spec [%]        | Disease associations        |
| <b>Myositis specific antibodies (MSA) *7</b>   |            |                 |                             |
| ● SRP  | 7          | high *          | PM, NAM, ASRPS (DM) 6, 33   |
| ● Mi-2   | 0 - 9      | high *          | DM, PM, IBM 6, 33, 62       |
| ● Alanyl-tRNA synthetase (PL12)  | up to 8    | high *          | PM, DM, ILD 6, 25           |
| ● Asparaginyl-tRNA synthetase (KS)   | < 1        | high *          | PM, DM, ILD 6               |
| ● Glycyl-tRNA synthetase (EJ)  | < 1        | high *          | PM, DM, ILD                 |
| ● Histidyl-tRNA synthetase (Jo-1)  | 19 - 33    | > 95 *          | PM, DM, ILD 6, 33, 25       |
| ● Isoleucyl-tRNA synthetase (OJ)   | < 1        | high *          | PM, DM, ILD 6               |
| ● Phenylalanyl-tRNA synthetase (ZO)  | unknown    | unknown         | PM, DM, ILD                 |
| ● Threonyl-tRNA synthetase (PL7)   | < 3        | high *          | PM, DM, ILD 6, 25           |
| ● Tyrosyl-tRNA synthetase (Ha, YRS)  | unknown    | unknown         | PM, DM, ILD                 |
| ● PMS1   | 8          | unknown         | DM, PM, aplA 8              |
| ● PMS2   | 4          | unknown         | DM, PM 8                    |
| ● MLH1   | 4          | unknown         | DM, PM 8                    |
| ● DNA-PK <sub>CS</sub>   | 2          | unknown         | DM, PM 8                    |
| ● Wa   | casuistics | unknown         | PM, ILD 30, 43              |
| ● KJ   | casuistics | unknown         | PM, ILD 55                  |
| ● Mas  | 1          | unknown         | DM, PM, AIH 6               |
| <b>Myositis associated antibodies (MAA) (see <a href="#">Dermatomyositis</a>)</b>                                  |            |                 |                             |
| ● PM/Scl   | up to 7    | medium          | DM, PM, OM 61, 48, 5, 6, 33 |
| <b>Other antibodies (see <a href="#">Dermatomyositis</a>)</b>  |            |                 |                             |
| * The figures of specificity refer to the idiopathic inflammatory myopathies on the whole (DM, PM, DM/PM-overlap). |            |                 |                             |
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## Autoantibodies in idiopathic inflammatory myopathies

### Antisynthetase syndrome

| Autoantibodies                      | Sens [%] | Spec [%] | Disease associations  |
|-------------------------------------|----------|----------|---|
| ● Histidyl-tRNA synthetase (Jo-1)   | 35,5     | *        | DM, PM, CADM, ILD <a href="#">6</a> , <a href="#">33</a> , <a href="#">25</a> |
| ● Glycyl-tRNA synthetase (EJ)       | 22,8     | *        | DM, PM, ILD, CADM   |
| ● Threonyl-tRNA synthetase (PL7)    | 17,5     | *        | DM, PM, ILD, CADM <a href="#">6</a> , <a href="#">25</a>                      |
| ● Alanyl-tRNA synthetase (PL12)     | 10,8     | *        | ILD, CADM, DM <a href="#">6</a> , <a href="#">25</a>                          |
| ● Asparaginy-tRNA synthetase (KS)   | 7,8      | *        | ILD, CADM <a href="#">6</a>   |
| ● Isoleucyl-tRNA synthetase (OJ)    | 4,5      | *        | ILD, PM, DM <a href="#">6</a>   |
| ● Phenylalanyl-tRNA synthetase (ZO) | unknown  | *        | PM, DM, ILD   |
| ● Tyrosyl-tRNA synthetase (Ha, YRS) | unknown  | *        | PM, DM, ILD   |
| ● SS-A/Ro 52                        | 18,6     | *        |   |
| ● SS-B/La                           | 2,4      | *        |   |
| ● Centromeres                       | 2,4      | *        |   |
| ● U1-snRNP                          | 1,2      | *        |   |
| ● Scl-70                            | < 1      | *        |   |
| ● Th/To                             | < 1      | *        |   |
| ● U3-snRNP                          | < 1      | *        |   |
| ● Sm                                | < 1      | *        |   |

\* The antisynthetase syndrome is defined by the presence of an autoantibody reacting with one of the tRNA-synthetases listed above. Indications of specificities therefore become superfluous. Shown is the prevalence of the various specificities of anti-synthetase antibodies in patients suffering from an antisynthetase syndrome ([23a](#)).

Symptoms: acute onset, fever, interstitial lung disease (ILD, 80 %), "mechanic hands" (70 %), Raynaud syndrome (40 %), polyarthritis (60 %), sometimes also erosive. A clinically manifest myositis may be lacking (amyopathic course), especially in the early stage and in association with PL7 and PL12 ([25](#)). The various specificities of the anti-synthetases are linked to different courses of disease and to different clinical manifestations.

According to Troyanov ([59](#)) classified as "overlap-myositis".

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## Autoantibodies in idiopathic inflammatory myopathies

### Necrotizing autoimmune myopathy (NAM)

| Autoantibodies                     | Sens [%] | Spec [%] | Disease associations  |
|------------------------------------|----------|----------|---|
| ● SRP 54 kDa * <sup>1</sup>        | 3        | high     | PM, DM, NAM <span style="float: right;">6, 33</span>            |
| ● SRP 68 kDa                       | < 1      | high     | PM, DM, NAM <span style="float: right;">24</span>               |
| ● SRP 72 kDa                       | < 1      | high     | PM, DM, NAM <span style="float: right;">24</span>               |
| ● 7 SL-RNA * <sup>2</sup>          | unknown  | unknown  | DP, PM <span style="float: right;">52</span>                    |
| ● HMG-CoA reductase * <sup>3</sup> | low      | high     | medication of statins <span style="float: right;">39, 40</span> |

\*<sup>1</sup> Anti-SRP may be associated with a rapidly progressive myopathy accompanied by muscle cell necrosis and scanty inflammatory infiltrations, sometimes with dermatomyositis like vascular lesions, showing decreased number of and enlarged capillaries and from time to time also complement deposits (**anti-SRP syndrome**). Rarely seen in children. Indicated frequencies refer on DM/PM. NAM may be associated with malignant tumors and virus infections (39)

According to Troyanov et al. (2005, 59) classified as "overlap-myositis".

\*<sup>2</sup> Anti-7SL-RNA were found mainly in Japanese patients positive for anti-SPP.

\*<sup>3</sup> Often associated with intake of statins. However, the majority of patients being on the medication of statins, also in cases of moderate incompatibility, do not develop antibodies against HMG-CoA reductase (63). Anti-HMG-CoA reductase is associated with DRB1\*1101.

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## Autoantibodies in idiopathic inflammatory myopathies

### DM/PM-Overlap-syndrome

| Autoantibodies                        | Sens [%]              | Spec [%] | Disease associations                          |
|---------------------------------------|-----------------------|----------|---|
| ● PM/Scl                              | 15 - 36               | high     | OM <a href="#">61, 48, 5, 6, 33, 16</a>       |
| ● Exosome <sup>*1</sup>               | unknown               | unknown  | OM <a href="#">5</a>                          |
| ● Ku <sup>*2</sup>                    | 4 - 25                | medium   | OM, DM, PM <a href="#">13, 33, 49, 18, 16</a> |
| ● Fibrillarin                         | 22                    | high     | OM <a href="#">33</a>                         |
| ● U5-snRNP                            | casuistics            | unknown  | OM <a href="#">36</a>                         |
| ● Histidyl-tRNA synthetase (Jo-1)     | 10 - 20               | high     | PM, DM, OM, ILD <a href="#">33, 64</a>        |
| ● Mi-2                                | 0 - 5 <sup>*1</sup>   | high     | PM, DM <a href="#">33, 64</a>                 |
| ● SRP                                 | 3                     | high     | PM, DM <a href="#">33</a>                     |
| <b>Other antibodies <sup>*3</sup></b> |                       |          |   |
| ● ANA- IIFT                           | bis 60                | low      | multiple                                      |
| ● Scl-70                              | 30 - 38               | high     | SSC, OM <a href="#">33</a>                    |
| ● Centromeres                         | 60 - 80               | high     | SSC, OM                                       |
| ● RNA polymerase                      | 22 - 30               | high     | SSC, OM                                       |
| ● Th/To                               | up to 13              | high     | SSC, OM                                       |
| ● U1-snRNP (U1-70K)                   | up to 21 <sup>*</sup> | low      | MCTD, SLE, SS <a href="#">6, 33, 10</a>       |
| ● U2-snRNP                            | up to 15 <sup>*</sup> | low      | <a href="#">11, 42</a>                        |
| ● SS-A/Ro 60                          | 4 <sup>*</sup>        | low      | SLE, SS                                       |
| ● SS-A/Ro 52                          | up to 37 <sup>*</sup> | low      | SS, SLE <a href="#">13, 6, 33</a>             |
| ● SS-B/La                             | up to 16 <sup>*</sup> | low      | SS, SLE <a href="#">6, 33</a>                 |
| ● ds-DNA                              | < 2 <sup>*</sup>      | 95       | SLE   |
| ● CCP                                 | 14 <sup>*</sup>       | > 90     | RA  |

DM/PM *overlap* syndromes: most frequently there are overlaps of DM/PM and systemic sclerosis in 40 - 50 % of cases ([59, 60](#)), less frequently are overlaps with SLE, MCTD, RA or antisynthetase and anti-SRP syndrome.

<sup>\*1</sup> Mainly in anti-PM/Scl positive patients. Antibodies found were directed against hRp4p, hRp40p, hRp41p, hRp42p, hR46p, hCsl4p ([5](#)).

<sup>\*2</sup> The antibodies are found in association with systemic sclerosis, Sjögren's syndrome, systemic lupus erythematosus ([49, 18](#)). Muscle necrosis and interstitial lung disease in 75 % of cases, also cortisol resistant. Antibodies may also be seen without accompanying myositis in SLE, SSC, RA, SS. About 8 % of anti-Ku positive patients manifest an isolated myositis ([38](#)).

<sup>\*3</sup> The listed antibodies constitute markers of the diseases shown under the heading "associated diseases. They can be found with varying prevalence also in patients showing DM/P-overlap syndromes. The figures of sensitivity and specificity of these antibodies refer to the systemic sclerosis, the figures tagged by <sup>\*</sup> refer to the DM/PM-overlap syndromes.

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## Autoantibodies in idiopathic inflammatory myopathies

### Cancer associated myositis

| Autoantibodies                  | Sens [%] | Spec [%] | Disease associations |
|---------------------------------|----------|----------|----------------------|
| ● TIF1- $\gamma$ * <sup>1</sup> | 13 - 30  | high     | JDM, ADM, CaM        |
| ● NXP2 (MJ) * <sup>2</sup>      | up to 30 | high     | JDM, ADM (CaM?)      |

\*<sup>1</sup> In 50 - 75 % associated with malignant tumors. Antibodies are also frequently seen in juvenile DM (in these cases not associated with malignant tumors), rarely in polymyositis. Associated tumors were carcinomas of breast, lung, pancreas and colon in USA (1), such as nasopharyngeal, breast, lung and cervix carcinomas in Taiwan (27).

\*<sup>2</sup> Anti-NXP2 are found in 19 - 29 % of patients with juvenile dermatomyositis, associated with pronounced muscle weakness, calcinosis, joint contractures, and muscle cell necroses (14, 23, 28). Their prevalence in early adult dermatomyositis in USA and Europe was 17 - 30 % (17, 9), in Japan only 1.6 % (28). In the adult form there were also found some associations with carcinomas and 8 % of the afflicted patients suffered from PM (9).

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## Autoantibodies in idiopathic inflammatory myopathies

| Inclusion body myositis (IBM)  |                          |                                 |   |
|--|--------------------------|---------------------------------|---|
| Autoantibodies   | Sens [%]                 | Spec [%]                        | Disease associations                                |
| ● Cytosolic 5'-Nukleosidase 1A (cN1A)  | 34                       | 98                              | IBM <span style="color: red;">37, 47</span>         |
| Myositis specific antibodies (MSA)   |                          |                                 |   |
| ● Histidyl-tRNA-Synthetase (Jo-1)  | 2 - 5 <sup>*1</sup>      |                                 | PM, DM <span style="color: red;">6, 51</span>       |
| ● Alanyl-tRNA-Synthetase (PL12)  | 4 <sup>*1</sup>          |                                 | PM, DM <span style="color: red;">51</span>          |
| ● SRP  | 0 - 3 <sup>*1</sup>      |                                 | PM, DM <span style="color: red;">6, 51</span>       |
| ● Mi-2   | 2 - 8 <sup>*1</sup>      |                                 | DM, PM <span style="color: red;">6, 51</span>       |
| Other antibodies   |                          |                                 |   |
| ● PM/Scl   | 12 <sup>*1</sup>         |                                 | OM <span style="color: red;">51</span>              |
| ● ANA-IIFT   | 29 <sup>*2</sup>         |                                 | multiple <span style="color: red;">51</span>        |
| ● ds-DNA   | 2                        |                                 | SLE <span style="color: red;">51</span>             |
| ● Rheumatoide factors  | casuistics <sup>*2</sup> |                                 | RA <span style="color: red;">31</span>              |
| ● Mitochondria (AMA)   | casuistics <sup>*2</sup> |                                 | PBC <span style="color: red;">31</span>             |
| ● SS-A/Ro 52   | 16 - 25 <sup>*2</sup>    |                                 | Kollagenosen <span style="color: red;">6, 51</span> |
| ● SS-A/Ro 60   | 4 - 6                    |                                 | Kollagenosen <span style="color: red;">6, 51</span> |
| ● SS-B/La  | 5 <sup>*2</sup>          |                                 | Kollagenosen <span style="color: red;">6, 51</span> |
| ● U1-snRNP   | 4 - 6                    |                                 | Kollagenosen <span style="color: red;">6, 51</span> |
| <sup>*2</sup> Also in association with overlap of Sjögren's syndrome and IBM <span style="color: red;">(31, 50)</span><br><sup>*1</sup> Not significant elevated in comparison with healthy controls <span style="color: red;">(51)</span> |                          |                                 |   |
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## Autoantibodies in idiopathic inflammatory myopathies

### Abbreviations

|      |             |
|------|-------------|
| Sens | Sensitivity |
| Spez | Specificity |

### Diseases

|       |                                       |
|-------|---------------------------------------|
| ASRPS | Anti-SRP syndrome                     |
| ADM   | Adult dermatomyositis                 |
| AIH   | Autoimmune hepatitis                  |
| aplA  | Aplastic anemia                       |
| CADM  | Clinically amyopathic dermatomyositis |
| CaM   | Cancer associated myositis            |
| DM    | Dermatomyositis                       |
| IBM   | Inclusion body myositis               |
| ILD   | Interstitial lung disease             |
| JDM   | Juvenile dermatomyositis              |
| NAM   | Necrotizing autoimmune myopathy       |
| MCL   | Mucocutaneous lesions                 |
| MCTD  | Mixed connective tissue disease       |
| OM    | Overlap-myositis                      |
| PBC   | Primary biliary cirrhosis             |
| PM    | Polymyositis                          |
| RA    | Rheumatoide Arthritis                 |
| SLE   | Systemic lupus erythematosus          |
| SS    | Sjögren's syndrome                    |
| SSC   | Systemic sclerosis                    |

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## Autoantibodies in idiopathic inflammatory myopathies

### Literature

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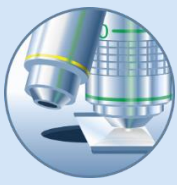
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